C. Mentoring Activities

Undergraduate Academic Advising

I continue to serve as an academic advisor to approximately 10-20 undergraduate students in each academic year. Also mentored Parks Scholars.

Direction of Undergraduate Research (in chronological order)

Student	Program	Period
Tiffany Tang	BS (NCSU)	F 2017 – present
Julia O'Brian[*]	BS (NCSU)	Su 2017
Asma Idries	BS (NCSU) – co-advised with D. Call	Mar. – May 2017
Rachel Scroggins	BS (NCSU) – co-advised with D. Call	Mar. – May 2017
Nancy Lee McLean[*]	BS (NCSU)	Sp 2017 – present
John Merrill[*,‡]	BS (NCSU)	Sp 2015 – present
Ally Patrick[*]	BS (NCSU)	Su 2014
Sara Troutman[*,☺]	BS (NCSU) – co-advised with Ranjithan	F 2013 – Sp 2015
Caroline LaFave	BS (NCSU)	Sp 2014
Rodniqua Minor[*,☺]	BS (NCSU)	Sp 2013 – Sp 2014
Justin Davenport[*,☺]	BS (NCSU)	Sp 2013 – Sp 2014
Dustin Rhodes[*]	BS (NCSU)	Sp/Su 2012
Benjamin Lord[‡]	BS (NCSU)	Sp 2012
Katie Dorety[*]	BS (NCSU)	Sp 2011
Evan Ged[*,☺]	BS (NCSU)	F 2010/Sp 2011
Ross Varin[*,☺,Δ]	BS (NCSU) – co-advised with de los Reyes	F 2010/Sp 2011
Ruth Small[*,☺]	BS (NCSU)	Sp 2010
Susan Dunn[*,☺,§]	BS (NCSU)	F 2009
Leigh-Ann Bender[*,☺]	BS (NCSU)	Sp/Su 2010
Maggie Hennessy[*,☺]	BS (NCSU)	Sp/Su 2009
Oksana Popovski[*,#,☺]	BS (NCSU)	Sp/Su 2009
Mary Waligora[*,‡,☺]	BS (NCSU)	Sp 2008 - Sp 2010
Martin Srb[*]	IAESTE[**]	Su 2007
Catherine M. Hoffman[*]	REU (NSF)	Su 2006
Laura E. Chambers[*,#]	REU (NSF)	Su/F 2003
Laurissa E. Hoyle[*,#,§]	REU (NSF)	F 2002/Sp 2003
Maria Pinzón[+]	Summer Research Experience (NSF)[&]	Su 2002
Travis B. Wagner[*,§]	BS (NCSU)	Sp/Su 2001
Anette Olsson[+]	BS (University of Lund, Sweden)	Sp 2001
Jon C. Williams[+,§]	BS (NCSU)	Su 2000/2001
Jun-Sang Lee[*]	BS (ChungBuk National Univ., S. Korea)	Su/Fall 1999
Jin-Man Kim[*]	BS (ChungBuk National Univ., S. Korea)	Su/F 1999
Patricia A. Quinlivan[*,§]	BS (NCSU)	Sp/Su 1999
Laurel E. Wright[*,§]	BS (NCSU)	Sp/Su 1999
Adrienne M. Sheats	Ravenscroft High School Intern	May 1999
Alper O. Savas[+,§]	BS (METU, Turkey)	Su 1998

Jenny Parmar[*, §]	BS (NCSU)	Sp 1998
Heather A. Marek[*]	REU (NSF)	Su 1997
Alper O. Savas[*, §]	BS (METU, Turkey)	Su 1997

[*] Students worked on externally funded projects
[©] Cost-shared with COE/CCEE undergraduate research funds
[Δ] Co-advised with F.L. de los Reyes
[#] Co-advised with M.A. Barlaz
[‡] Student was recipient of an NCSU undergraduate research award
[**] International Association for the Exchange of Students for Technical Experience
[§] Students subsequently enrolled in the graduate Civil Engineering program at NCSU
[+] Students worked on unfunded projects to collect screening data for research proposals
[&] The North Carolina Minority Graduate Education Program is funded by NSF and includes the "Intensive Research and Training Program," which has two primary components: the "Academic Year Research Experience" (ARE) and the "Summer Research Experience" (SRE).

Graduate Committees (Chair/co-chair)

Student	**Degree**	**Committee Role**	**Graduation Date**
S. Park	PhD	co-chair	anticipated Sp 22
C. Zhang	PhD	chair	anticipated Sp 20
A. McElroy[^]	PhD	chair	anticipated Sp 18
Z. Hopkins	PhD	chair	anticipated Sp 17
B. Yuncu	PhD	chair	Fa 10
J. M. Saquing	PhD	co-chair	Fa 09
A. A. Rossner	PhD	chair	Fa 08
A. C. Baeza[*,+]	PhD	chair	Fa 08
C. Chun	PhD	co-chair	Su 07
Y. Chen	PhD	co-chair	Su 03
L. Li	PhD	co-chair[§]	Su 02
B. Wu	PhD	co-chair[§]	Su 02

[^] GAANN Fellow
[*] NSF Graduate Research Fellow
[+] NWRI Fellow
[§] I served as primary research advisor, but I was not able to chair PhD committees because of my associate membership in the Graduate Faculty

M. Fitzstevens	MS	co-chair	anticipated Su 18
O. Hounwanou	MS	chair	anticipated Sp 18
C. Maness	MS	chair	Sp 17
C. Lopez Velandia	MS	chair	Su 16
J. Moreno Barbosa	MS	chair	Su 16
R. S. Ingham	MS	chair	Su 14
A. C. Greune	MS	chair	Su 14
V. U. Edeback	MS	chair	Su 14
E. C. Arevalo	MS	chair	Sp 14
A. M. Reinert	MS	chair	Sp 13
M. E. Fotta	MS	chair	Su 12
L. M. Dudley	MS	chair	Sp 12

S. E. Dunn[*, +]	MS	chair	Fa 11
A. Mastropole	MS	chair	Su 11
Q. Deng	MS	chair	Su 10
A. Viswakumar	MS	chair	Sp 10
V. Mandapaka	MS	co-chair	Fa.08
I. A. Mezzari[+]	MS	chair	Sp.06
L. A. Mitchell	MS	chair	Sp.05
A. A. Rossner	MS	chair	Su.04
T. B. Wagner	MS	chair	Su.03
P. A. Quinlivan[*]	MS	chair	Su.01
C. M. Taylor	MS	chair	Sp.00
S. R. Gandy	MS	chair	Sp.00
N. Rastogi	MS	chair	Fa.99
R. C. Belk	MS	chair	Sp.99
D. S. Briley[+]	MS	chair	Fa.98
A. H. Rike	MS	chair	Sp.98

[*] NSF Graduate Research Fellow
[+] Thesis Award Winner (AWWA, AEESP)

Graduate Committees (Member)

Student	**Program**	**Graduation Status**
A. Hess	PhD (Process Eng. – ETH Zurich)	ongoing
Q. Cheng	PhD (CE)	ongoing
M. Bentley	PhD (CE – U. Colorado, Boulder)	ongoing
A. Beciragic	PhD (ESE – UNC-CH)	ongoing
H. Chmielewski	PhD (OR)	ongoing
B. Hess	PhD (BAE)	ongoing
K. Grzebyk	PhD (ESE – UNC-CH)	ongoing
J.M. Tillotson	PhD (CE)	ongoing
S. Safavizadeh	PhD (CE)	completed
E. Gillispie	PhD (SSC)	completed
K. Shimabuku	PhD (CE – U. Colorado, Boulder)	completed
E. Bailey	PhD (ESE – UNC-CH)	completed
J. Kearns	PhD (CE – U. Colorado, Boulder)	completed
J. Won	PhD (CE)	completed
J.R. Lang	PhD (CE)	completed
A.D. Lindsay	PhD (NE)	completed
X. Wang	PhD (CE)	completed
F. de la Cruz	PhD (CE)	completed
D. Kempisty	PhD (CE – U. Colorado, Boulder)	completed
A. Kennedy	PhD (CE – U. Colorado, Boulder)	completed
A. Sobremisana	PhD (CE)	completed
X. He	PhD (CE)	completed
J. Oh	PhD (CE)	completed
Q. Chow	PhD (CE – U. Illinois, Urbana)	completed

C. Corwin	PhD (CE – U. Colorado, Boulder)	completed
S. M. Alpert	PhD (CE)	completed
S. Velten	PhD (CE – ETH Zurich)	completed
T. M. Kunberger	PhD (CE)	completed
C. Mota	PhD (CE)	completed
I. Lou	PhD (CE)	completed
M. Badruzzaman	PhD (CE – Ariz. State)	completed
L. Schideman	PhD (CE – U. Illinois, Urbana)	completed
D. Liu	PhD (CE)	completed
Y. Liu	PhD (CE)	completed
E. Solano	PhD (CE)	completed
K. Clay	MS (MEAS)	completed
J. Babuin-Nickels	MS (MEAS)	completed
A. Berglund	MS (CE)	completed
J. B. Wahlen	MS (CE)	completed
S. R. Farling	MS (CE)	completed
F. J. Hurley	MS (CE)	completed
K. Fogle	MS (CE)	completed
B. Karami	MS (CE)	completed
J. Lang	MS (CE)	completed
L. Bao	MS (CE)	completed
J. P. Kaplan	MS (ESE – UNC-CH)	completed
M. Vazquez	MS (CE)	completed
E. Gallimore	MS (CE)	completed
C. Bowker	MS (CE)	completed
R. Prevost	MS (CE)	completed
Y. Bi	MS (Soil Science)	completed
L. Wellborn	MS (CE)	completed
K. Jang	MS (CE)	completed
J. H. Martin II	MS (BAE)	completed
V. L. Nguyen	MS (CE)	completed
A. Sadri	MS (CE)	completed
G. Gulez	MS (CE)	completed
J. C. Williams	MS (CE)	completed
C. Long	MS (CE)	completed
N. Bartholomew	MS (Soil Science)	completed
A. C. Baeza	MS (CE)	completed
J. Liao	MS (CE)	completed
D. C. Hopkins	MS (CE)	completed
J. C. Ihnatolya	MS (CE)	completed
V. A. Ortiz	MS (CE)	completed
K. M. Aragona	MS (CE)	completed
R. J. Fairweather	MS (CE)	completed
D. M. Giachini	MS (CE)	completed
D. K. Peplinski	MS (CE)	completed
M. T. Pelton	MS (CE)	completed

J. K. Rash	MS (CE)	completed
M. R. Sanchez	MS (CE)	completed
J. B. Stillman	MS (CE)	completed
M. B. Vergonio	MS (CE)	completed

MCE Project Advisor

I. A. Mezzari	MCE	Sp.09
A. O. Savas	MCE	Sp.03
J. M. Chambers	MCE	Fa.99
G. C. Rucker	MCE	Sp.97

External PhD Thesis Reviewer

Lionel Ho	University of South Australia	Fall 2004

Graduate Academic Advising

In addition to the MS and PhD students, for whom I serve as research and academic advisor, I continue to serve as an academic advisor to approximately 2 MCE students (courses-only program) and 2 MCEZ students (Engineering Online program) in each academic year.

Hosting of Visiting Scholars

Zihong Fan, Lecturer, Chongqing Technology and Business University, March 2017 – August 2018. Research Topic: Cyclodextrin-enhanced adsorption of disinfection by-product precursors.

Mary Jo Weiss-Errico, PhD Student, Florida International University, January-February 2018. Research Topic: Functionalization of graphene oxide for targeted PFAS removal.

Geert Aschermann, PhD Student, TU Berlin, November 2017 – February 2018. Research Topic: Factors controlling PFAS desorption from activated carbon.

Josh Kearns, PhD Student, CU-Boulder; Director, Aqueous Solutions (A non-profit organization with the mission to enable households and communities to ensure the safety of their drinking water in a sustainable and self-reliant manner.) April – October 2008, Jan. 2013-May 2017. Research Topic: Effect of char preparation on adsorptive pesticide removal from drinking water.

Guangqian Wu, PhD Student and Lecturer, Nanjing Forestry University, June 2014-March 2015. Research Topic: Adsorption of 1,4-dioxane on graphene and carbonaceous resins.

Dr. Zhang Hua, Assistant Professor from Tongji University, August 2011 – August 2012. Research Topic: Organic contaminant sorption to municipal solid waste constituents. Co-directed by Drs. Barlaz and Knappe

Dr. Qingdong Qin, post-doctoral researcher at Southeast University in Nanjing, China. Dr. Qin spent 6 months at NCSU to conduct research on activated carbon adsorption processes. April – September 2011.

Dr. Koichi Ohno, Assistant Professor, Laboratory of Environmental Risk Engineering, Hokkaido University, Sapporo, Japan. Dr. Ohno spent a 10-month sabbatical at NCSU and conducted research on activated carbon adsorption processes. March 2009 – January 2010.

Silvana Velten, PhD Candidate, EAWAG (Swiss Federal Institute of Aquatic Science and Technology), February – August 2007. Research Topic: The effects of natural organic matter preloading on physicochemical properties of granular activated carbon and polar organic contaminant removal efficiency.

Dr. Hang-Bae Jun, Assistant Professor, ChungBuk National University, South Korea, January 1999 – January 2000. Research Topic: Optimization of Coagulation Conditions for the Removal of Algae from Drinking Water. Funding Agency: Korean Science and Engineering Foundation. The collaboration resulted in the publication of one peer-reviewed paper. Dr. Jun was promoted to Associate Professor at ChungBuk University after his stay at NC State University.

Advising of Post-Doctoral Research Associates

Dr. Nadine Kotlarz, August 2017 – present. Research Topics: Human biomarkers for emerging PFASs; water treatment options for emerging PFASs

Dr. Yue Zhi, August 2017 – present. Research Topic: Nanoparticles for the recovery of phosphate from waste

Dr. Mei Sun, April 2013 – December 2015. Research Topics: Adsorptive removal of fluorinated alternatives from drinking water, biological sulfide potential. Co-directed by Drs. Barlaz and Knappe. Current position: Assistant Professor, University of North Carolina at Charlotte.

Dr. Jovita Saquing, August 2009 – August 2010. Research Topic: Contaminant Fate and Transport in Municipal Solid Waste. Co-directed by Drs. Barlaz and Knappe. Current position: Post-doctoral research associate, University of Delaware.

Dr. Erik Rosenfeldt, August 2006 – July 2007. Research Topic: New Techniques to Quantify Assimilable Organic Carbon Concentrations and Microbial Regrowth in Drinking Water Distribution Systems. Current position: Director of Applied Research, Hazen and Sawyer.

Dr. Shannon Bartelt-Hunt, July 2004 – December 2005. Research Topic: Assessment of the Behavior of Chemical and Biological Contaminants in Landfills. Co-directed by Drs. Barlaz and Knappe. Current position; Professor, University of Nebraska at Omaha.

Advising of Student Groups

I have served and continue to serve as research group advisor and technical advisory committee member for the NCSU Student Chapter of Engineers Without Borders. Fall 2006 – present.

Master's and Doctoral Theses Directed and Being Directed

PhD Theses

1. Bingyan Wu. 2002. Factors controlling alkylbenzene sorption and desorption in municipal solid waste. Ph.D. Thesis (co-chair with Dr. M.A. Barlaz).*

2. Lei Li. 2002. Effects of activated carbon surface chemistry and pore structure on the adsorption of trace organic contaminants from aqueous solution. Ph.D. Thesis (co-chair with Dr. M.A. Barlaz).*

3. Ye Chen. 2003. Effects of Aging on the Bioavailability of Toluene Sorbed to Municipal Solid Waste Components. Ph.D. Thesis (co-directed with Dr. M.A. Barlaz)

4. Chen Chun. 2007. Quantifying Anti-Strip Additive in Asphalt Binders and Mixes. Ph.D. Thesis (co-directed with Dr. A.A. Tayebali).

5. A. Carolina Baeza. 2008. Removal of pharmaceutical and endocrine disrupting chemicals by sequential photochemical and biological oxidation processes. Ph.D. Thesis (Carolina Baeza's work was supported by a NSF Graduate Research Fellowship and a NWRI fellowship).

6. Alfred A. Rossner. 2008. Removal of polar and emerging organic contaminants by alternative adsorbents. Ph.D. Thesis.

7. Jovita Saquing. 2009. Sorption Behavior and Persistence of Organic Contaminants in Landfills. Ph.D. Thesis (co-directed with Dr. M.A. Barlaz).

8. Bilgen Yuncu. 2010. Removal of 2-Methylisoborneol and Geosmin by High-Silica Zeolites and Powdered Activated Carbon in the Absence and Presence of Ozone. Ph.D. Thesis.

9. Zachary Hopkins. Expected 2017. Advanced oxidation and reduction processes for the control of emerging ether contaminants in drinking water (tentative title). Ph.D. Thesis.

10. Amie McElroy. Expected 2018. Degradation of 1,4-dioxane by monooxygenase-producing microorganisms (tentative title). Ph.D. Thesis.

11. Chuhui Zhang. Expected 2020. Total oxidizable precursor assay for the characterization of environmental samples contaminated with perfluoroalkyl ether acids (tentative title). PhD Thesis.

12. Sol Park. Expected 2022. Electrically assisted adsorption of short-chain perfluoroalkyl acids.

* I served as primary research advisor, but I was not able to chair PhD committees because of my associate membership in the Graduate Faculty

MS Theses

1. Andrew H. Rike. 1998. The impacts of algae and extracellular organic matter on coagulant demand and trihalomethane and dichloroacetonitrile formation potential. M.S. Thesis.

2. David S. Briley. 1999. Optimization of coagulation conditions for the removal of algae in conventional water treatment. M.S. Thesis. (David Briley's thesis received 2nd place in the AEESP/Montgomery Watson Master's Thesis Award Competition).

3. Robert C. Belk. 1999. On-line monitoring tools for detecting algae in natural waters. M.S. Thesis.

4. Neerja Rastogi. 1999. Effects of Potassium Permanganate Preoxidation on Algae Removal and Finished Water Quality. M.S. Thesis.

5. Steven R. Gandy. 2000. Effectiveness of Dissolved Air Flotation and Microsand-Enhanced Flocculation for the Removal of Algae from Drinking Water. M.S. Thesis.

6. Caleb M. Taylor. 2000. Relationships between Physical and Chemical Characteristics of Municipal Solid Waste and its Sorptive Properties. M.S. Thesis. (co-directed with Dr. M.A. Barlaz)

7. Patricia A. Quinlivan. 2001. The Effects of Activated Carbon Surface Chemistry and Pore Structure on the Adsorption of Methyl Tertiary-Butyl Ether and Trichloroethene from Natural Water. M.S. Thesis. (Patricia Quinlivan's work was supported by a NSF Graduate Research Fellowship).

8. Travis B. Wagner. 2003. Factors controlling hydrophobic organic contaminant sorption to and desorption from municipal solid waste. M.S. Thesis. (co-directed with Dr. M.A. Barlaz)

9. Alfred A. Rossner. 2004. Adsorption of methyl tertiary-butyl ether on high-silica zeolites: effects of adsorbent characteristics and natural organic matter on adsorption isotherms. M.S. Thesis.

10. Lisa A. Mitchell. 2005. Factors controlling desorption rates of hydrophobic organic contaminants from municipal solid waste. M.S. Thesis.

11. Isabella A. Mezzari. 2006. Predicting the adsorption capacity of activated carbon for organic contaminants from fundamental adsorbent and adsorbate properties. M.S. Thesis. (Isabella Mezzari's thesis received 2nd place in the 2007 AWWA Academic Achievement Awards Master's Thesis Competition).

12. Venkata Mandapaka. 2008. Effect of prolonged heating on asphalt-aggregate bond strength. M.S. Thesis (co-directed with Dr. A.A. Tayebali).

13. Anjali Viswakumar. 2010. Development of a gas chromatography-tandem mass spectrometry method for the simultaneous analysis of 19 taste and odor compounds. M.S. Thesis.

14. Qianru Deng. 2010. Removal of biochemically active compounds by powdered activated carbon adsorption processes. M.S. Thesis.

15. Angela Mastropole. 2011. Evaluation of available scale-up approaches for the design of GAC contactors. M.S. Thesis.

16. Susan Dunn. 2011. Effect of powdered activated carbon base material and size on disinfection by-product precursor and trace organic pollutant removal. M.S. Thesis.

17. Leigh-Ann Dudley. 2012. Removal of perfluorinated compounds by powdered activated carbon, superfine powdered activated carbon, and anion exchange resins. M.S. Thesis.

18. Meredith Fotta. 2012. Effect of granular activated carbon type on adsorber performance and scale-up approaches for volatile organic compound removal. M.S. Thesis.

19. Allison Reinert. 2013. Granular activated carbon adsorption of micropollutants from surface water: Field-scale adsorber performance and scale-up of bench-scale data. M.S. Thesis.

20. Elisa Arevalo. 2014. Removal of Perfluorinated Compounds by Anion Exchange: Factors Affecting Resin Performance and Regeneration. M.S. Thesis.

21. Rachel Ingham. 2014. Henry's Law and Freundlich adsorption constants for carcinogenic volatile organic contaminants. M.S. Thesis.

22. Viking Edeback. 2014. Treatment Options for Disinfection Byproduct Control in Drinking Water Sources with Elevated Bromide Levels. M.S. Thesis.

23. Amber Greune. 2014. Bromide Occurrence in North Carolina and the Relationship between Bromide Concentration and Trihalomethane Formation. M.S. Thesis.

24. Jonathan Moreno Barbosa. 2016. Evaluation of Freundlich Adsorption Constants for VOCs at Regulatory Relevant Concentrations. M.S. Thesis.

25. Catalina Lopez Velandia. 2016. Occurrence of 1,4-dioxane in the Cape Fear River Watershed and Effectiveness of Point-Of-Use Treatment Options for 1,4-dioxane Control. M.S. Thesis.

26. Clark Maness. 2017. Control of Regulated and Unregulated Disinfection Byproducts by Granular Activated Carbon : Effects of Bromide, Iodide, and Pre-Chlorination. M.S. Thesis.

27. Obatayo Hounwanou. Effect of soil properties on turbidity control strategies for stormwater treatment (tentative title). M.S. Thesis. Expected August 2018.

III. SCHOLARSHIP IN THE REALMS OF FACULTY RESPONSIBILITY

A. Scholarly Accomplishments

Book Chapters

1. Summers, R.S.; D.R.U. Knappe; and V.L. Snoeyink. "Chapter 14 – Adsorption of Organic Compounds." In *Water Quality and Treatment*, 6th ed., J.K. Edzwald (Ed.), McGraw-Hill: New York, NY, 2011.

2. Knappe, D.R.U. "Chapter 9 - Surface Chemistry Effects in Activated Carbon Adsorption of Industrial Pollutants." In *Interface Science in Drinking Water Treatment – Theory and Applications*, Newcombe, G. and Dixon, D. (Eds.), Academic Press: Oxford, UK, 2006.

Refereed Journal Publications

1. Hopkins, Z.R., Sun, M., DeWitt, J.R., and Knappe, D.R.U. "Recently detected drinking water contaminants: GenX and other per- and polyfluoroalkyl ether acids." *Journal AWWA*, accepted (invited).

2. Hess, B.J.; P. Kolar, J.J. Classen, D. Knappe, and J.J. Cheng. "Evaluation of waste eggshells for adsorption of copper from water." *Transactions of the ASABE*, accepted.

3. Kennedy, A.M., Reinert, A.R., Knappe, D.R.U., and Summers, R.S. "Prediction of Full-Scale GAC Adsorption of Organic Micropollutants." *Environmental Engineering Science*, 34(7): 496-507, 2017.

4. Sun, M., Arevalo, E., Strynar, M.J., Lindstrom, A.B., Richardson, M., Kearns, B., Smith, C., Pickett, A., and Knappe, D.R.U. "Legacy and Emerging Perfluoroalkyl Substances Are Important Drinking Water Contaminants in the Cape Fear River Watershed of North Carolina." *Environmental Science and Technology Letters*, 3(12): 415-419, 2016.

5. Sun, M., Lopez-Velandia, C., Knappe, D.R.U. "Determination of 1,4-dioxane in the Cape Fear River watershed by heated purge-and-trap preconcentration and gas chromatography–mass spectrometry." *Environmental Science and Technology*, 50(5): 2246–2254, 2016.

6. Kearns, J.P.; Knappe, D.R.U.; and Summers, R.S. "Feasibility of using traditional kiln charcoals in low cost water treatment: The role of pyrolysis conditions on 2,4-D herbicide adsorption." *Environmental Engineering Science*, 32(11): 912-921, 2015.

7. Kearns, J.P.; Shimabuku, K.K.; Mahoney, R.B.; Knappe, D.R.U.; and Summers, R.S. "Meeting multiple water quality objectives through treatment using locally generated char: Improving organoleptic properties and removing synthetic organic contaminants and disinfection byproducts." *Journal of Water, Sanitation and Hygiene for Development*, 5(3): 359-372, 2015.

8. Kennedy, A.M.; Reinert, A.M.; Knappe, D.R.U.; Ferrer, I.; and Summers, R.S. "Full- and pilot-scale GAC adsorption of organic micropollutants." *Water Research*, 68: 238-248, 2015.

9. Lindsay, A.; Byrns, B.; King, W.; Andhvarapou, A.; Fields, J.; Knappe, D.; Fonteno, W.; and Shannon, S. "Fertilization of radishes, tomatoes, and marigolds using a large-volume atmospheric glow discharge." *Plasma Chemistry and Plasma Processing*, 34(6): 1271-1290, 2014.

10. Kearns, J.P.; Wellborn, L.S.; Summers, R.S.; and Knappe, D.R.U. "2,4-D adsorption to biochars: effect of preparation conditions on equilibrium adsorption capacity and comparison with literature data for activated carbons." *Water Research*, 62: 20-28, 2014.

11. Kearns, J.P.; Knappe, D.R.U.; and Summers, R.S. "Synthetic organic water contaminants in developing communities: An overlooked challenge addressed by adsorption with locally generated char." *Journal of Water, Sanitation and Hygiene for Development*, 4(3): 422-436, 2014.

12. Kovalova, L.; Knappe, D.R.U.; Lehnberg, K., Kazner, K., and Hollender, J. "Removal of highly polar micropollutants from wastewater by powdered activated carbon." *Environ. Sci. Poll. Res.*, 20(6): 3607-3615, 2013.

13. Chen, Y.; D.R.U. Knappe; and M.A. Barlaz. "The Effect of Aging on the Bioavailability of Toluene Sorbed to Municipal Solid Waste Components." *Chemosphere*, 90(2): 251-259, 2013.

14. Matsui, Y.; Yoshida, T.; Nakao, S.; Knappe, D.R.U.; and Matsushita, T. "Characteristics of Competitive Adsorption between 2-Methylisoborneol and Natural Organic Matter on Superfine and Conventionally Sized Powdered Activated Carbons." *Water Research*, 45(16): 4741-4749, 2012.

15. Saquing, J.M.; D.R.U. Knappe; and M.A. Barlaz. "Fate and Transport of Phenol in a Packed Bed Reactor Containing Simulated Solid Waste." *Waste Management*, 32(2): 327-334, 2012.

16. Baeza, A.C. and D.R.U. Knappe. "Transformation Kinetics of Biochemically Active Compounds in Low-Pressure UV Photolysis and UV/H_2O_2 Advanced Oxidation Processes." *Water Research*, 45(15): 4531-4543, 2011.

17. Velten, S.; D.R.U. Knappe; J. Traber; H.P. Kaiser; U. von Gunten; M. Boller; and S. Meylan. "Characterization of natural organic matter adsorption in granular activated carbon adsorbers." *Water Research*, 45(13): 3951-3959, 2011.

18. Saquing, J.M.; C.D. Saquing; D.R.U. Knappe; and M.A. Barlaz. "Impact of Plastics on Fate and Transport of Organic Contaminants in Landfills." *Environmental Science and Technology* 44(16): 6396-6402, 2010.

19. Alpert, S.M.; D.R.U. Knappe; and J.J. Ducoste. "Modeling the UV/hydrogen peroxide advanced oxidation process using computational fluid dynamics." *Water Research*, 44(6):

1797-1808, 2010.

20. Saquing, J.M.; L.A. Mitchell; Wu, B.; T.B. Wagner; D.R.U. Knappe; and M.A. Barlaz. "Factors controlling alkylbenzene and tetrachloroethene desorption from municipal solid waste components." *Environmental Science and Technology* 44(3): 1123-1129, 2010.

21. Rosenfeldt, E.J.; C. Baeza; and D.R.U. Knappe. "Application of a Flow Cytometry Method to Assess the Bacterial Quality of Drinking Water." *Journal AWWA*, 101(10): 60-70, 2009.

22. Rossner, A.; S.A. Snyder; and D.R.U. Knappe. "Removal of an emerging contaminant mixture by alternative adsorbents." *Water Research*, 43(15): 3787-3796, 2009.

23. Teuten, E.L.; J.M. Saquing; D.R.U. Knappe; M.A. Barlaz; S. Jonsson; A. Björn; S.J. Rowland; R.C. Thompson; T.S. Galloway; R. Yamashita; D. Ochi; Y. Watanuki; M.P. Zakaria; Y. Ogata; H. Hirai; S. Iwasa; K. Mizukawa; Y. Hagino; A. Imamura; M. Saha; and H. Takada. "Transport and release of chemicals from plastics to the environment and to wildlife." *Philosophical Transactions of The Royal Society B*, 364: 2027-2045, 2009.

24. Rossner, A. and D.R.U. Knappe. "MTBE adsorption kinetics on alternative adsorbents and packed bed adsorber performance." *Water Research*, 42(8/9): 2287-2299, 2008.

25. Bartelt-Hunt, S.L.; D.R.U. Knappe; and M.A. Barlaz. "A review of chemical warfare agent simulants for the study of environmental behavior." *Critical Reviews in Environmental Science and Technology* 38(2): 112-136, 2008.

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4. Hopkins, Z. and Knappe, D.R.U. Treatment Of 1,4-Dioxane In Surface Water By Ozone And Advanced Oxidation Processes. AWWA Annual Conference. Philadelphia, PA, June 11-14, 2017.

5. Knappe, D.R.U., Dudley, L.A., Arevalo, E., Strynar, M., Lindstrom, A., and PFAS Removal by Activated Carbon Adsorption & Anion Exchange. AWWA Annual Conference. Philadelphia, PA, June 11-14, 2017.

6. Sun, M., Dudley, L.A., Arevalo, E., Strynar, M., Lindstrom, A., and Knappe, D.R.U. Removal of traditional and emerging perfluoroalkyl substances by powdered activated carbon adsorption and anion exchange. AWWA Water Quality Technology Conference. Indianapolis, IN, November 13-17, 2016.

7. Cuthbertson, A.A., Kimura, S.Y., Richardson, S.D., Knappe, D., Seidel, C., Summers, R.S., Stanford, B., and Dickenson, E. Use of Granular Activated Carbon (GAC) for Controlling Emerging Disinfection By-Products (DBPs). AWWA Water Quality Technology Conference. Indianapolis, IN, November 13-17, 2016.

8. Castellano, L., Hopkins, Z., and Knappe, D.R.U. Analysis of 1,4-dioxane and carcinogenic VOCs at sub-mg/L levels by gas chromatography-triple quadrupole mass spectrometry. AWWA Water Quality Technology Conference. Indianapolis, IN, November 13-17, 2016.

9. Sun, M., L.A. Dudley, M. Strynar, A. Lindstrom, and D. Knappe. "Adsorption of traditional and emerging perfluoroalkyl substances by powdered activated carbon." *251st ACS National Meeting*, San Diego, CA, March 13-17, 2016.

10. Knappe, D., C. Lopez-Velandia, Z. Hopkins, and M. Sun. "Occurrence of 1,4-dioxane in North Carolina surface water and evaluation of possible treatment options." *251st ACS National Meeting*, San Diego, CA, March 13-17, 2016.

11. Sun, M., C. Lopez-Velandia, and D.R.U. Knappe. Using heated purge-and-trap and gas chromatography-mass spectrometry to quantify 1,4-dioxane in the Cape Fear River watershed in North Carolina. AWWA Water Quality Technology Conference. Salt Lake City, UT, November 15-19, 2015.

12. Dunn, S.E., A. Viswakumar, B. Yuncu, D. Rhodes, E. Ged, and D.R.U. Knappe. "Superfine powdered activated carbon for the removal of disinfection byproduct precursors and organic micropollutants. AWWA Water Quality Technology Conference. Salt Lake City, UT, November 15-19, 2015.

13. Moreno-Barbosa, J., K. Porter, J. Collins, J. Roccaro, and D. Knappe. "Implications of potential new regulatory scenarios for the removal of carcinogenic volatile organic compounds by granular activated carbon." North Carolina AWWAWEA Annual Conference. Raleigh, NC, November 16, 2015. Received 1st Prize in the Best Poster Award Competition and was therefore invited for presentation at the *AWWA Annual Conference* in Chicago, June 19-22, 2016.

14. Lopez-Velandia, C., M. Sun, and D.R.U. Knappe. "1,4-Dioxane: Occurrence and treatment options for an emerging surface water contaminant." North Carolina AWWAWEA Annual Conference. Raleigh, NC, November 16, 2015. Received 2nd Prize in the Best Poster Award Competition.

15. Lopez-Velandia, C., M. Sun, and D.R.U. Knappe. "1,4-Dioxane: Occurrence, sources, and treatment options for an emerging surface water contaminant." SETAC North America 36th Annual Meeting. Salt Lake City, UT, November 1-5, 2015.

16. Sun, M.*, E. Arevalo, L.A. Dudley, A.B. Lindstrom, M.J. Strynar, and D.R.U. Knappe. "Adsorption of perfluoroalkyl substances, including a fluorinated alternative, by powdered activated carbon." FLUOROS 2015 An International Symposium on Fluorinated Organics in the Environment. Golden, CO, July 12-14, 2015.

17. Stanford, B.D.*, A.M. Reinert, E. Rosenfeldt, M. Bishop, and D.R.U. Knappe. "A Hybrid Approach to Granular Activated Carbon: A Model to Balance Cost with Water Quality Objectives and DBP Compliance." AWWA Annual Conference, Anaheim, CA, June 5-8, 2015.

18. C. Lopez-Velandia*, M. Sun, and D.R.U. Knappe. "1,4-Dioxane Occurrence in the Cape Fear River Watershed of North Carolina and Point-of-Use Treatment Options for 1,4-Dioxane Control." NSF WORKSHOP: Fostering Advances in Water Resource Protection and Crisis Communication, Lessons Learned from Recent Disasters. Sheperdstown, WV, May 27-29, 2015.

19. M. Sun* and D.R.U. Knappe. "Rapid Analysis of 1,4-Dioxane in Water by Heated Purge-and-Trap Gas Chromatography-Mass Spectrometry." NSF WORKSHOP: Fostering Advances in Water Resource Protection and Crisis Communication, Lessons Learned from Recent Disasters. Sheperdstown, WV, May 27-29, 2015.

20. Chmielewski, H.*, S. Troutman, D.R.U. Knappe, and R. Ranjithan. "Modeling Future Performance of Water Pumping and Treatment Options." World Environmental & Water Resources Congress, Austin, TX, May 17-21, 2015.

21. A.B. Lindstrom*, M.J. Strynar, R.L. McMahen, L. McMillan, and D.R.U. Knappe. "Municipal Waste Water Treatment Plant Biosludge Applications and Perfluoroalkyl Acid Surface Water Contamination in North Carolina." NCAWWA-WEA 14th Annual Spring Conference, Wilmington, NC, April 12-14, 2015.

22. Lopez-Velandia, C., M. Sun, and D.R.U. Knappe. "1,4-Dioxane - A Contaminant of Emerging Concern for NC Drinking Water Providers." *WRRI Annual Conference*, Raleigh, NC, March 18-19, 2015.

23. A.B. Lindstrom*, A.B., M.J. Strynar, L. McMillan, D. Knappe, E. Arevalo, S. Wing, A. Lowman, M. Serre, and P. Jat. "Surface Disposal of Waste Water Treatment Plant Biosoilds – an Important Source of Perfluorinated Compound Contamination in the Environment?" SETAC North America, Vancouver, BC, Canada, November 9-13, 2014.

24. Arevalo, E.C.*, L.A. Dudley, A.M. Reinert, M. Strynar, A. Lindstrom, L. McMillan, and D.R.U. Knappe. "Occurrence of Perfluorinated Compounds in the Cape Fear River Basin and Effectiveness of Treatment Approaches." *93rd NC AWWA/WEA Annual Conference*, Concord, NC. November 10-13, 2013. Received 1st Prize in the Best Poster Award Competition and was therefore invited for presentation at the *AWWA Annual Conference* in Boston, June 8-12, 2014.

25. Chmielewski, H.*, Troutman, S., Knappe, D. & Ranjithan, R. "Optimizing Multiple Objectives in Future Water Treatment and Distribution Decisions." 16th Annual Water Distributions Systems Analysis Symposium at the World Environmental & Water Resources Congress, Portland, OR, June 1-5, 2014.

26. Ingham, R.* and D.R.U. Knappe. "Henry's Law Constants and Freundlich Adsorption Constants for Carcinogenic Volatile Organic Compounds." *WRRI Annual Conference*, Raleigh, NC, March 19-20, 2014.

27. Greune, A.C.* and D.R.U. Knappe. "Bromide Occurrence in North Carolina Surface Waters." *93rd NC AWWA/WEA Annual Conference*, Concord, NC. November 10-13, 2013.

28. Edeback, V.U.* and D.R.U. Knappe. "Use of Rapid Small-Scale Column Tests to Assess Full Scale Granular Activated Carbon Adsorber Design Options for Disinfection Byproduct Precursor Control." *93rd NC AWWA/WEA Annual Conference*, Concord, NC. November 10-13, 2013.

29. Ingham, R.* and D.R.U. Knappe. "Evaluation of Henry's Law Constants for Carcinogenic Volatile Organic Compounds." *93rd NC AWWA/WEA Annual Conference*, Concord, NC. November 10-13, 2013.

30. Dudley, L.A., Q. Deng, P. Kaplan, Y. Liu, H. Weinberg, and D.R.U. Knappe*. "Removal of Emerging Contaminants with Water Treatment Processes Commonly Used in North Carolina." *WRRI Annual Conference*, Raleigh, NC, March 20-21, 2013

31. Fotta, M.E.*, J. Roccaro, and D.R.U. Knappe. "Effect of Carbon Type, Reactivation, and Empty Bed Contact Time on Granular Activated Carbon Performance for Volatile Organic Compound Removal." *South Carolina Environmental Conference*, Myrtle Beach, SC, March 10, 2013.

32. Reinert, A.* and D.R.U. Knappe. "Comparing Scale-Up Approaches to Predict Granular Activated Carbon Adsorber Performance for Micropollutant Removal." *92nd NC AWWA/WEA Annual Conference*, Raleigh, NC. November 11-14, 2012. Received 2nd Prize in the Best Poster Award Competition.

33. Chowdhury, Z.*, J. Shaw, D.R.U. Knappe, J. Roccaro, K. Randazzo, and A. Roberson. "What are the Impacts of a cVOC Group Regulation?" *AWWA Water Quality Technology Conference*, Toronto, ON, Nov. 4-7, 2012.

34. Fotta, M.E.*, J. Roccaro, and D.R.U. Knappe. "Effect of Activated Carbon Type on Scale-Up of Adsorbers for Volatile Organic Compound Removal from Groundwater." *AWWA Annual Conference*, Dallas, TX, June 10-14, 2012.

35. Dudley, L.M.*, M. Strynar, A. Lindstrom, L. McMillan, and D.R.U. Knappe. "Removal of perfluorinated compounds by powdered activated carbon and anion exchange resins." *2012 WRRI Annual Conference and NCWRA Symposium*, Raleigh, NC. March 27-28, 2012. Received 3rd Prize in the Best Poster Award Competition.

36. Dudley, L.M., M. Strynar, A. Lindstrom, L. McMillan, and D.R.U. Knappe*. "Removal of perfluorinated compounds by powdered activated carbon: Effect of base material and particle size." *AWWA Water Quality Technology Conference*, Phoenix, AZ, Nov. 13-17, 2011.

37. Fotta, M.E.*, A. Reinert*, and D.R.U. Knappe. "Evaluation of Scale-Up Approaches for the Design of Granular Activated Carbon Contactors." *91st NC AWWA/WEA Annual Conference*, Concord, NC. November 13-16, 2011.

38. Dudley, L.M.*, M. Strynar, A. Lindstrom, L. McMillan, and D.R.U. Knappe. "Removal of Perfluorinated Compounds by Powdered Activated Carbon: Effect of Base Material and Particle Size." *91st NC AWWA/WEA Annual Conference*, Concord, NC. November 13-16, 2011.

39. Mastropole, A.*, Fotta, M., Kennedy, A., Thurman, M.E., Ferrer, I., Summers, R.S., and Knappe, D.R.U. "Scale-Up Approaches for the Design of GAC Contactors: Emerging Contaminant Mixtures at Environmentally Relevant Concentrations." *AWWA Annual Conference*, Washington, DC, Jun. 12-16, 2011.

40. Dunn, S.E.* and D.R.U. Knappe. "Effect of powdered activated carbon base material and size on disinfection byproduct precursor removal." *Engineering Day at the NC Legislature*, Raleigh, NC. April 27, 2011. Winning poster in the Grand Challenges Competition for Providing Access to Clean Water. Also winner of People's Choice Award.

41. Ged, E.* and D.R.U. Knappe. "Effectiveness of superfine powdered activated carbon for the removal of sulfamethoxazole." *20th Annual NC State Undergraduate Research Symposium*, Raleigh, NC. April 12, 2011. Poster was selected as one of four winners in the Engineering category.

42. Dunn, S.E.* and D.R.U. Knappe. "Effect of powdered activated carbon base material and size on disinfection byproduct precursor removal." *2011 WRRI Annual Conference and NCWRA Symposium*, Raleigh, NC. March 22-23, 2011. Received 2nd Prize in the Best Poster Award Competition.

43. Dudley, L.M., Q. Deng, M. Hennessy, and D.R.U. Knappe*. "Treatment Options for the Removal of Emerging Pollutants of Concern." *2011 WRRI Annual Conference and NCWRA Symposium*, Raleigh, NC. March 22-23, 2011.

44. Deng, Q., K. Ohno, and D.R.U. Knappe. "Removal of pharmaceuticals from drinking water by powdered activated carbon." *89th NC AWWA/WEA Annual Conference*, Raleigh, NC. November 15-18, 2009.

45. B. Yuncu and D.R.U. Knappe. "Removal of taste and odor compounds in drinking water with zeolite-enhanced ozonation." *89th NC AWWA/WEA Annual Conference*, Raleigh, NC. November 15-18, 2009. Received 1st Prize in the Best Poster Award Competition.

46. Waligora, M.C. and D.R.U. Knappe. "Starch-based polymers as a green coagulant aid alternative for the treatment of drinking water." *89th NC AWWA/WEA Annual Conference*, Raleigh, NC. November 15-18, 2009.

47. I.A. Mezzari,* J. Saquing, D.R.U. Knappe, and M.A. Barlaz. "Development of a Fate and Transport Model for Organic Chemicals in Landfills." *The 5th Intercontinental Landfill Research Symposium*, Copper Mountain Conference Center, CO, Sept. 10-12, 2008.

48. M. Srb,* C. Baeza, and D.R.U. Knappe. "Kinetics of Sulfonamide Removal by Low-Pressure UV Photolysis and UV/H_2O_2 Advanced Oxidation Processes. *IWA World Water Congress and Exhibition*, Vienna, Austria, Sept. 7-12, 2008.

49. S. Velten,* D.R.U. Knappe, and M. Boller. "Effects of Natural Organic Matter Preloading on Physical Characteristics and Remaining MTBE Adsorption Capacity of Granular Activated Carbon." *IWA World Water Congress and Exhibition*, Vienna, Austria, Sept. 7-12, 2008.

50. D.R.U. Knappe* and C. Baeza. "UV/H_2O_2 Oxidation of Antimicrobial Compounds: Biochemical Activity and Biodegradability of Oxidation Intermediates." *5th IWA Leading-Edge Conference & Exhibition on Water & Wastewater Technologies*, Zurich, Switzerland, June 1-4, 2008.

51. B. Yuncu and D.R.U. Knappe.* "Use of high-silica zeolites for the targeted removal of taste and odor compounds from drinking water." *235th ACS National Meeting*, New Orleans, LA, April 6-10, 2008.

52. R.S. Summers,* D. Dani; B. Zachman; C. Corwin; N. Blute; M. McGuire; and D.R.U. Knappe. "MTBE Adsorption: Evaluating EBCT, competition, and fouling." *235th ACS National Meeting*, New Orleans, LA, April 6-10, 2008.

53. C. Baeza* and D.R.U. Knappe. "Removal of antimicrobial compounds and their associated biochemical activity by UV photolysis and UV/H_2O_2 processes." *233rd ACS National Meeting*, Chicago, IL, March 25-29, 2007. In *Abstracts of Papers of the American Chemical Society – Division of Environmental Chemistry*, Vol. 47, No. 1.

54. Rossner, A.* and D.R.U. Knappe. "MTBE adsorption kinetics on alternative adsorbents and packed bed adsorber performance." *233rd ACS National Meeting*, Chicago, IL, March 25-29, 2007. In *Abstracts of Papers of the American Chemical Society – Division of Environmental Chemistry*, Vol. 47, No. 1.

55. Mezzari, I.A.; T.F. Speth; and D.R.U. Knappe.* "Prediction of organic contaminant adsorption isotherms on activated carbons." *233rd ACS National Meeting*, Chicago, IL, March 25-29, 2007. In *Abstracts of Papers of the American Chemical Society – Division of Environmental Chemistry*, Vol. 47, No. 1.

56. Rossner, A.; S.A. Snyder; and D.R.U. Knappe.* "Adsorption of emerging organic contaminant mixtures by alternative adsorbents." *233rd ACS National Meeting*, Chicago, IL, March 25-29, 2007. In *Abstracts of Papers of the American Chemical Society – Division of Environmental Chemistry*, Vol. 47, No. 1.

57. Mezzari, I.A.* and D.R.U. Knappe. "Predicting the Adsorption Capacity of Activated Carbon for Emerging Organic Contaminants from Fundamental Adsorbent and Adsorbate Properties." *86th NC AWWA/WEA Annual Conference*, Greensboro, NC. November 12-15, 2006. (Poster won 1st place in best poster competition).

58. Rossner, A.* and D.R.U. Knappe. "Adsorption kinetics of MTBE on alternative adsorbents." *86th NC AWWA/WEA Annual Conference*, Greensboro, NC. November 12-15, 2006.

59. Bartelt-Hunt, S. L., Barlaz, M. A., Knappe, D. R. U. and P. Kjeldsen. "Fate of Chemical Warfare Agents and Toxic Industrial Chemicals in Landfills," *4th Intercontinental Landfill Research Symposium*, Gallivare, Sweden, June 14 – 16, 2006.

60. Baeza, C.* and D.R.U. Knappe. "Removal of an Antimicrobial Compound by Sequential Photochemical and Biological Oxidation Processes." *85th NC AWWA/WEA Annual Conference*, Greensboro, NC. November 13-16, 2005. (Poster won 2nd place in best poster competition).

61. D.R.U. Knappe.* "Activated Carbon Characteristics and the Prediction of Aqueous-Phase Adsorption Isotherms." Invited presentation at the *230th ACS National Meeting*, Washington, DC, August 28 – September 1, 2005.

62. Bartelt-Hunt, S. L.*, Barlaz, M. A., Knappe, D. R. U. and P. Kjeldsen. "Assessment of the Behavior of Chemical Warfare Agents in Landfills." *AEESP Frontiers Conference*, Potsdam, NY, July 25 – 27, 2005.

63. Barlaz, M. A., Bartelt-Hunt, S. L., Knappe, D. R. U. and P. Kjeldsen. "Assessment of the Behavior of Chemical Warfare Agents in Landfills." *SWANA Landfill Symposium*, Boulder,

CO, June 6 – 9, 2005.

64. Chen, Y., Knappe, D. R. U. and M. A. Barlaz.* "The Effect of Aging on the Bioavailability of Toluene Sorbed to Municipal Solid Waste Components," *The 3rd Intercontinental Landfill Research Symposium*, Lake Toya, Japan, Nov. 30 – Dec. 2, 2004.

65. Rossner, A.A.* and D.R.U. Knappe. "Adsorption of MTBE on Alternative Adsorbents." *83rd NC AWWA/WEA Conference*, Greensboro, NC, Nov. 16-19, 2003.

66. Knappe, D.R.U. *; L. Li; P.A. Quinlivan; and G. Newcombe. "Recent Advances in Characterizing GAC Performance." Invited presentation at the IWA-sponsored *Global Conference on Leading Edge Water and Wastewater Treatment Technologies*, Noordwijk/Amsterdam, The Netherlands, May 26-28, 2003.

67. Zhang, Z.*; M.A. Barlaz; and D.R.U. Knappe. "Factors Affecting the Bioavailability of Tetrachloroethylene Sorbed to Municipal Solid Waste Components." *103rd General Meeting of the American Society for Microbiology*, Washington, DC, May 18-22, 2003.

68. Chen, L. *; M.A. Nanny; D.R.U. Knappe; T.B. Wagner; and N. Ratasuk. "Chemical Characterization and Sorption Capacity of Degraded Newsprint from a Landfill." *225th ACS National Meeting*, New Orleans, LA, March 23-27, 2003. In *Abstracts of Papers of the American Chemical Society – Division of Environmental Chemistry*, Vol. 43, No. 1.

69. Wu, B.; D.R.U. Knappe *; and M.A. Barlaz. "Modeling Toluene Desorption from Municipal Solid Waste Components." *2002 Fall Meeting of the American Geophysical Union*, San Francisco, CA, December 6-10, 2002.

70. Zhang, Z.; L.E. Hoyle; D.R.U. Knappe*; and M.A. Barlaz. "Interactions between Hydrophobic Organic Contaminants and Dissolved Organic Matter in Methanogenic Leachate." *2nd Intercont. Landfill Research Symposium*, Asheville, NC, Oct. 13-16, 2002.

71. Zhang, Z.*; M.A. Barlaz; and D.R.U. Knappe. "Factors Affecting the Bioavailability of Tetrachloroethene Sorbed to Municipal Solid Waste Components." *2nd Intercontinental Landfill Research Symposium*, Asheville, NC, Oct. 13-16, 2002.

72. Wu, B., Knappe, D. R. U. and M. A. Barlaz. "Factors Controlling Alkylbenzene Sorption and Desorption to Municipal Solid Waste." *2nd Intercontinental Landfill Research Symposium*, Asheville, NC, Oct. 13-16, 2002.

73. Chen, Y. *; M.A. Barlaz; and D.R.U. Knappe. "Effect of Aging on the Bioavailability of Toluene Sorbed to Municipal Solid Waste Components." *Bioremediation and Biodegradation - Current Advances in Reducing Toxicity, Exposure and Environmental Consequences*, Pacific Grove, CA, June 9-12, 2002.

74. Knappe, D.R.U. * and L. Li. "Predicting the Adsorption Capacity of Activated Carbon from Fundamental Adsorbent and Adsorbate Properties." Invited presentation at the *IWA Workshop on Biological Activated Carbon Filtration*. Delft, The Netherlands, May 29-31,

2002.

75. Knappe, D.R.U.*; L. Li; and P.A. Quinlivan. "Activated Carbon Surface Chemistry and Pore Structure Effects on Adsorption of Volatile Organic Compounds from Natural Water." *2001 World Water Congress*, Berlin, Germany, October 15-19, 2001. (Abstract accepted for platform presentation, but trip was cancelled as a result of the Sept. 11 tragedies).

76. Newcombe, G.*; J. Morrison; C. Hepplewhite ; and D.R.U. Knappe. "Predicting PAC Doses for the Removal of Algal Metabolites: How Can NOM Characterization Techniques Help Us?" *AwwaRF/Cooperative Research Centre for Water Quality and Treatment/Vivendi Workshop: Relating NOM Characteristics to Improve Water Treatment Process Selection and Performance*, Berlin, Germany, October 10-12, 2001.

77. Li, L.*; P.A. Quinlivan; and D.R.U. Knappe. "Effects of Activated Carbon Surface Chemistry and Pore Structure on the Adsorption of MTBE from Natural Water." *222nd ACS National Meeting*, Chicago, IL, August 26-30, 2001. In *Abstracts of Papers of the American Chemical Society – Division of Environmental Chemistry*, Vol. 41, No. 2.

78. Wu, B.*; C.M. Taylor; D. R.U. Knappe; M.A. Barlaz; and M.A. Nanny. "Factors Controlling Alkylbenzene Sorption to Municipal Solid Waste." *222nd ACS National Meeting*, Chicago, IL, August 26-30, 2001. In *Abstracts of Papers of the American Chemical Society – Division of Environmental Chemistry*, Vol. 41, No. 2.

79. Wu, B.; C.M. Taylor; M.A. Barlaz; D.R.U. Knappe*; and M.A. Nanny. "Effects of Anaerobic Sorbent Degradation on the Sorption of Toluene and *o*-Xylene to municipal solid waste components." *2001 International Containment & Remediation Technology Conference and Exhibition*, Orlando, FL, June 10-13, 2001.

80. Barlaz, M.A. and D.R.U. Knappe*. "The Effects of Aging and Sorbent Decomposition on the Bioavailability of Toluene and *o*-Xylene in Solid Waste." *1999 US EPA Bioremediation Research Program Review*, Bloomingdale, IL, Nov. 2-4, 1999.

81. Barlaz, M.A.*; F.D. Sanin; and D.R.U. Knappe. "The Fate of Toluene and Dichloroethane in a Superfund Landfill." *In Situ and On-Site Bioremediation 5th International Symposium*, San Diego, CA, April 19-22, 1999.

82. Rastogi, N.; S.R. Gandy; and D.R.U. Knappe*. "Removal of Algae from Drinking Water by Conventional Treatment and Microsand-Enhanced Flocculation." *Annual NC Water Resources Research Conference*, Raleigh, NC, March 25, 1999.

83. Sanin, F.D.; M.A. Barlaz; and D.R.U. Knappe*. "Toluene Sorption, Humification, and Biodegradation in Excavated Refuse, a High Organic Carbon Sorbent." *AGU Spring Meeting*, Boston, MA, May 26-29, 1998.

84. Knappe, D.R.U.* "Strategies for Algae Removal in Drinking Water Treatment." *Annual NC Water Resources Research Conference*, Raleigh, NC, April 1, 1998.

85. Knappe, D.R.U. *; Y. Matsui; V.L. Snoeyink; P. Roche; M.J. Prados; and M.M. Bourbigot. "Predicting the Adsorption Capacity of Powdered Activated Carbon for Micropollutants." *American Carbon Society Workshop: Carbon Materials for the Environment*, Charleston, SC, June 9-12, 1996.

86. Snoeyink, V.L.* and D.R.U. Knappe. "Optimal Use of Powdered Activated Carbon for Pesticide Removal." *Second EPA National Drinking Water Treatment Technology Transfer Workshop*, Kansas City, MO, August 12-14, 1996.

87. Knappe, D.R.U. *; V.L. Snoeyink; F.S. Cannon; and R.G. Lee. "The Effect of Calcium on the Thermal Regeneration of Granular Activated Carbon." *AWWA Annual Conference*, Philadelphia, PA, June 23-27, 1991.

* indicates presenter

Invited Presentations

1. Knappe, D.R.U. Impacts of fluorochemical production and use on drinking water quality in North Carolina. University of Rhode Island, Kingston, RI, April 20, 2018.

2. Sun, M., Arevalo, E., Strynar, M., Lindstrom, A., and Knappe, D.R.U. Occurrence and control of legacy and emerging perfluoroalkyl substances in North Carolina. *255th ACS National Meeting*, New Orleans, LA, March 18-22, 2018. (Awards Session)

3. Knappe, D.R.U., Rossner, A.A., Dudley, L.A., and Sun, M. Factors controlling the adsorption of ionizable organic compounds to activated carbon. *255th ACS National Meeting*, New Orleans, LA, March 18-22, 2018.

4. Sun, M., Lopez-Velandia, C., McElroy, A., and Knappe, D.R.U. Rapid and sensitive method for the determination of 1,4-dioxane analysis in a wide range of aqueous matrices. *255th ACS National Meeting*, New Orleans, LA, March 18-22, 2018.

5. Hopkins, Z., Merrill, J., Sun, M., Arevalo, E., Lindstrom, A., Strynar, M., and Knappe, D.R.U. Impacts of perfluoroalkyl ether acids on drinking water quality in North Carolina. Emerging Contaminants Summit. Westminster, CO, March 6-7, 2018.

6. Knappe, D.R.U. Impacts of fluorochemical production and use on drinking water quality in North Carolina. University of Colorado – Boulder, Boulder, CO, October 6, 2017.

7. Sun, M., Arevalo, E., Dudley, L.A., Strynar, M., Lindstrom, A., and Knappe, D.R.U. Legacy and emerging per- and polyfluoroalkyl substances are challenging small (and large) surface water treatment systems in North Carolina. 14th Annual USEPA Drinking Water Workshop Cincinnati, OH, August 22, 2017

8. Knappe, D.R.U., Mezzari, I.A., and Speth, T.F. Combining the Polanyi-Dubinin-Manes framework with molecular models to predict adsorption isotherms of aqueous organic

contaminants on activated carbons. *252nd ACS National Meeting*, Philadelphia, PA, August 21-25, 2016.

9. Dudley, L.A., Sun, M., Arevalo, E., Lindstrom, A., Strynar, M., and Knappe, D.R.U. Factors controlling the adsorption of perfluoroalkyl substances by powdered activated carbon. *252nd ACS National Meeting*, Philadelphia, PA, August 21-25, 2016.

10. Greune, A. and Knappe, D.R.U. Effect of bromide discharges on source water bromide levels and disinfection by-product formation in North Carolina. *252nd ACS National Meeting*, Philadelphia, PA, August 21-25, 2016.

11. Knappe, D.R.U. Keynote: Activated carbon adsorption processes in the USA: Developments in research and application. Workshop: Adsorption in der Wasseraufbereitung: Renaissance einer bewährten Technologie, 27. Mülheimer Wassertechnisches Seminar, Mülheim, Germany, June 15, 2016.

12. Knappe, D.R.U. Water treatment options for perfluoroalkyl substances. Tsinghua University, Beijing, China, May 25, 2016.

13. Knappe, D.R.U., L.A. Dudley, E. Arevalo, M. Sun, M. Strynar, and A. Lindstrom. Water treatment options and challenges for perfluoroalkyl substances and fluorinated alternatives. *251st ACS National Meeting*, San Diego, CA, March 13-17, 2016.

14. Knappe, D. "Polanyi-Dubinin-Manes model framework to predict adsorption isotherms of aqueous organic contaminants on activated carbons." *37th International Activated Carbon Conference*, Orlando, FL, February 25-26, 2016.

15. Knappe, D. "Considerations for large and small utilities for addressing emerging contaminants from upstream sources." *Freshwater in the North Carolina Coastal Plain: Understanding and Preparing for 21st Century Challenges*. New Bern, NC, February 19, 2016.

16. Knappe, D.R.U.*, L.A. Dudley, E. Arevalo, A.B. Lindstrom, and M.J. Strynar. "Adsorption of perfluoroalkyl substances by powdered activated carbon." Clemson University, March 13, 2015.

17. Knappe, D.R.U. Carcinogenic volatile organic contaminant (cVOC) group rule. Charlotte Water Training Institute, Charlotte, NC, February 5, 2015.

18. Knappe, D.R.U. UCMR3 Update for North Carolina. Charlotte Water Training Institute, Charlotte, NC, February 5, 2015.

19. Knappe, D.R.U. Thoughts about the safety of our drinking water: Emerging surface water quality and drinking water treatment challenges in North Carolina Lunch and learn, West Raleigh Rotary Club, Oct. 17, 2014.

20. Knappe, D.R.U. Unregulated Data Communications Workshop - Recent North Carolina Research and Associated Data. City of Raleigh, Sept. 16, 2014.

21. Knappe, D.R.U. UCMR3 Update for North Carolina. NCWOA 2014 Remote Lab Tech Day, Winston-Salem, NC, August 27, 2014.

22. Knappe, D.R.U.*, A.C. Greune, and V.E. Edeback. "Uncovering the Trends of Increasing Bromide in North Carolina's Surface Waters: Sources and Impacts on Brominated DBPs throughout the State." In *Proc. of the AWWA Annual Conference*, Boston, MA, Jun. 8-12, 2014.

23. Knappe, D.R.U. Emerging surface water quality and water treatment challenges in North Carolina. CCEE Department Lunch and Learn, June 5, 2014.

24. Knappe, D.R.U.* and J. Fireline. "Fracking 101 - Shale Gas Extraction using Horizontal Drilling and Hydraulic Fracturing." *NC-AWWA/WEA Lab Technology Day*, Raleigh, NC, May 6, 2014.

25. Knappe, D.R.U. Adsorptive Removal of Micropollutants from Drinking Water Using Granular Activated Carbon and Superfine Powdered Activated Carbon. Technical University of Dresden, Germany, May 28, 2013,

26. Knappe, D.R.U. Adsorptive Removal of Micropollutants from Drinking Water Using Granular Activated Carbon and Superfine Powdered Activated Carbon. Technical University of Berlin, May 24, 2013.

27. Knappe, D.R.U.* and J. Fireline. "Bromide Occurrence in the Cape Fear River Basin." *Triad Area Utilities Meeting*, Greensboro, NC, April 11, 2013.

28. Knappe, D.R.U.* and J. Fireline. "Fracking 101 - Shale Gas Extraction using Horizontal Drilling and Hydraulic Fracturing." *92nd NC AWWA/WEA Annual Conference*, Raleigh, NC. November 11-14, 2012.

29. Knappe, D.R.U. "Disinfection byproducts in drinking water: Human health risks and risk management options." Genetic and Environmental Mutagenesis Society (GEMS) Meeting, Research Triangle Park, NC. April 24, 2012.

30. Knappe, D.R.U. "Control of Disinfection Byproduct Formation with Activated Carbon." Disinfection Byproducts Workshop, NC Public Water Supply Section, Division of Water Resources, Raleigh, NC. April 19, 2012.

31. Knappe, D.R.U. "Suffolk County Water Authority VOC Case Study." AWWA Carcinogenic Volatile Organic Contaminant Workshop, Suffolk County Water Authority, Long Island, NY. March 28, 2012.

32. Knappe, D.R.U. "Granular Activated Carbon Adsorption: Opportunities for Process Optimization." Suffolk County Water Authority, Long Island, NY. June 16, 2011.

33. Knappe, D.R.U. "Algal Performance Issues for Water Treatment Plants." Emerging Water Quality Issues Committee - Algae Workshop, AWWA Annual Conference, Washington, DC. June 12, 2011.

34. Knappe, D.R.U. "Emerging Contaminants and Water Scarcity – Perspectives from North Carolina and Beyond." Keynote address – Emerging Contaminants Research: Implications for Water Treatment, Wastewater Treatment, and Utility Planning. Hazen & Sawyer Workshop, Cary, NC. February 17, 2011.

35. Knappe, D.R.U. "Staying Ahead of the Curve – Advanced Treatment Technologies for Water Reuse." Public Health – Reclaim to Sustain Workshop, NCAWWA-WEA, Raleigh, NC, Mar. 9, 2010

36. Knappe, D.R.U. "Disinfection byproducts: Do current regulatory approaches in the U.S. effectively reduce risk?" Workshop EULA 2010, Universidad de Concepcion, Concepcion, Chile, January 8, 2010.

37. Knappe, D.R.U. "Treatment Options for Water Reclamation." Invited presentation, Public Health & Reclaimed Water Workshop, NC DENR, Raleigh, NC, Aug. 27, 2009.

38. Knappe, D.R.U. "Removal of Pharmaceuticals and EDCs by Oxidation and Adsorption." Invited seminar, Dept. of Environmental and Molecular Toxicology, NC State University, Raleigh, NC, Oct. 14, 2008.

39. Knappe, D.R.U. "Removal of Pharmaceuticals and Endocrine Disrupting Chemicals by Oxidation and Adsorption." *NC/GA/SC Watershed Symposium & Drinking Water Technology Forum*, Concord, NC, Sept. 17-19, 2008.

40. Knappe, D.R.U. "Adsorptive and Oxidative Removal of Trace Organic Pollutants." Invited seminar at the Technologiezentrum Wasser, University of Karlsruhe, Germany, May 29, 2008.

41. Knappe, D.R.U. "Emerging Issues and Technologies in Water and Wastewater Treatment." Invited presentation, WRRI Advisory Committee Meeting, Raleigh, NC, May 13, 2008.

42. Knappe, D.R.U.* "Activated Carbon Characteristics That Matter for Organic Micropollutant Removal from Drinking Water." Invited presentation at the workshop "Advances in the Use of Activated Carbon." *AWWA Water Quality Technology Conference*, Charlotte, NC, Nov. 4-8, 2007.

43. Knappe, D.R.U.* "Removal of Wastewater-Derived Organic Contaminants and Their Associated Biochemical Activity by Low Pressure UV/H_2O_2 Treatment." Invited presentation at the workshop "Advanced Oxidation Technologies in Water Treatment: Fundamentals and Applications." *AWWA Water Quality Technology Conference*, Charlotte,

NC, Nov. 4-8, 2007.

44. Knappe, D.R.U.* "Activated Carbon Characteristics and the Prediction of Aqueous-Phase Adsorption Isotherms." Invited presentation at the *230th ACS National Meeting*, Washington, DC, August 28-September 1, 2005.

45. Knappe, D.R.U.* "*A priori* Prediction of Adsorption Isotherms on Activated Carbons." Invited seminar, Dept. of Civil and Environmental Engineering, University of Illinois, Urbana, April 25, 2006.

46. Knappe, D.R.U.* "Activated Carbon Adsorption Processes – Effects of Adsorbent Properties on the Removal of Trace Organic Contaminants." Invited lecture, Dept. of Urban Environmental Engineering, Hokkaido University, June 2, 2005.

47. Knappe, D.R.U.* "Predicting Adsorption Isotherms from Fundamental Adsorbent and Adsorbate Properties." Invited presentation at EAWAG: Swiss Federal Institute for Environmental Science and Technology, Dübendorf, Switzerland, June 3, 2004.

48. Knappe, D.R.U.* "Strategies for Algae Detection and Removal in Water Treatment." Invited presentation at the Jordan Lake Stakeholder Meeting, NC A&T State University, Greensboro, NC, January 29, 2004.

49. Knappe, D.R.U.*; L. Li; P.A. Quinlivan; and G. Newcombe. "Recent Advances in Characterizing GAC Performance." Invited presentation at the IWA-sponsored *Global Conference on Leading Edge Water and Wastewater Treatment Technologies*, Noordwijk/Amsterdam, The Netherlands, May 26-28, 2003.

50. Glasgow, H.B.*; J.M. Burkholder; B.W. Touchette; L.C. Ehrlich; D.R.U. Knappe; and E.H. Allen. "Impacts of Toxigenic Cyanobacteria on North Carolina Waterways." Invited Presentation at a NCDENR and NCPH-sponsored workshop entitled *Blue Green Algae and Public Water Supplies*, Hickory, NC, February 19, 2003; Asheville, NC, February 25, 2003; Statesville, NC, February 26, 2003.

51. Knappe, D.R.U. * and L. Li. "Predicting the Adsorption Capacity of Activated Carbon from Fundamental Adsorbent and Adsorbate Properties." *IWA Workshop on Biological Activated Carbon Filtration*. Delft, The Netherlands, May 29-31, 2002.

52. "Teleconference on Taste & Odor in Drinking Water: Operational Tools and Techniques for Identification and Control." University of North Carolina at Chapel Hill, May 21, 2001.

53. Knappe, D.R.U. * "Strategies for Algae Detection and Algae Removal in Water Treatment." Duke University, Durham, NC, February 26, 2001.

54. Knappe, D.R.U. *; D.S. Briley; and N. Rastogi. "Optimized Treatment to Minimize the Impacts of Algae on Finished Water Quality." *Annual NC AWWA & WEA Conference*, Research Triangle Park, NC, November 8-11, 1998.

55. Knappe, D.R.U. *; D.S. Briley; and N. Rastogi. "Optimized Treatment to Minimize the Impacts of Algae on Finished Water Quality." *Conference of the Canadian Water and Wastewater Association*, Quebec City, Quebec, October 28-30, 1998.

56. "Teleconference on Adsorption and Membrane Treatment Technologies: Applications to Water Utilities in North Carolina." UNC-Chapel Hill, July 24, 1997.

* indicates presenter

Honors and Awards

1. Advisor for the 1st and 2nd prize winners at the student poster award competition at the *97th NCAWWA/WEA Annual Conference*, November 2017.

2. Best paper award for our 2016 publication "Legacy and Emerging Perfluoroalkyl Substances Are Important Drinking Water Contaminants in the Cape Fear River Watershed of North Carolina" in *ES&T Letters*, 2017

3. Advisor for the 3rd prize winner in Engineering at the NCSU Graduate Research Symposium, March 23, 2016.

4. Advisor for the 1st and 2nd prize winners at the student poster award competition at the *95th NCAWWA/WEA Annual Conference*, November 2015.

5. NSF Science Nation video of our 1,4-dioxane research in the Cape Fear River watershed, 2015

6. Advisor for the 1st prize winner at the student poster award competition at the *93rd NCAWWA/WEA Annual Conference*, 2013.

7. Thesis advisor for the 1st place winner in the 2013 American Water Works Association Academic Achievement Award competition for the best Master's Thesis (Annual national competition. Award was given for Susan Dunn's MS thesis entitled "Effect of powdered activated carbon base material and size on disinfection by-product precursor and trace organic pollutant removal").

8. Advisor for the 2nd prize winner at the student poster award competition at the *92nd NCAWWA/WEA Annual Conference*, 2012.

9. Advisor for the 3rd prize winner at the student poster award competition at the *WRRI Annual Conference and NCWRA Symposium*, 2012.

10. Thank a Teacher Recipient, Fall 2011.

11. Outstanding Teacher Award, NC State University, 2011.

12. Advisor for a winning poster at the *20th Annual NC State Undergraduate Research Symposium*, 2011.

13. Winning poster in the Grand Challenges Competition for Providing Access to Clean Water, College of Engineering, NC State University, 2011. Poster was also winner of People's Choice Award at Engineering Day at the NC Legislature.

14. Advisor for the winner of the Best Student Paper Award at the American Water Works Association Water Quality Technology Conference, 2007

15. Thesis advisor for the 2nd place winner in the 2007 American Water Works Association Academic Achievement Award competition for the best Master's Thesis (Annual national competition. Award was given for Isabella Mezzari's MS thesis entitled "Predicting the adsorption capacity of activated carbon for organic contaminants from fundamental adsorbent and adsorbate properties").

16. AWWA Water Science & Research Division Best Poster Award, 2006 (Award for best research poster at the Annual AWWA Conference and Exhibition)

17. Bill Horn Kimley-Horn Faculty Award for excellence in graduate and undergraduate teaching and other accomplishments, Department of Civil, Construction, and Environmental Engineering, NC State University, 2003.

18. AWWA Water Science & Research Division Best Paper Award, 2001 (Annual award presented by the American Water Works Association for the best research paper published in Journal AWWA – the award was given for the paper entitled "Atrazine Removal by Preloaded GAC" that appeared in the October 1999 issue).

19. Young Civil Engineer Achievement Award, University of Illinois, 2000 (Annual award presented by the University of Illinois Civil and Environmental Engineering Alumni Association to three outstanding alumni).

20. Thesis advisor for the 2nd place winner in the 1999 AEESP/Montgomery Watson Master's Thesis Award Competition (Annual national competition. Award was given for David Briley's MS thesis entitled "Optimization of coagulation conditions for the removal of algae in conventional water treatment").

B. Research Project Record

Sponsored Research

1. **Title:** Assessing Impact Of Drinking Water Exposure To Genx (hexafluoropropylene Oxide Dimer Acid) In The Cape Fear River Basin, North Carolina. PI: Hoppin, J. Co-PIs: Smart, R.; Knappe, D.; May, K. Agency: National Institute of Environmental Health Sciences

(NIEHS) ($311,399; 11/1/17-10/31/18).

2. **Title:** Collaborative Research: Eager: Tailored Sorbents For The Removal Of Emerging Per- And Polyfluorinated Alkyl Substances From Water. PI: Knappe, D.R.U. Agency: National Science Foundation ($35,000; 9/15/17-8/31/18). An equal amount of funding was awarded to Kevin O'Shea, Dept. of Chemistry, Florida International University.

3. **Title:** Electrically Assisted Sorption and Desorption of Per- and Polyfluoroalkyl Substances. PI: Call, D. Co-PI: Knappe, D.R.U. Agency: Strategic Environmental Research and Development Program ($200,000; 5/16/18-5/16/19).

4. **Title:** Field Demonstration and Comparison of Ex-Situ Treatment Technologies for Poly- and Perfluoroalkyl substances (PFASs) in Groundwater. PI. Knappe, D.R.U. Agency: Water Research Foundation (Prime: Department of Defense)($200,011; 5/16/18-5/16/20).

5. **Title:** Center for Human Health and the Environment. PI: Smart, R.C. Co-PIs: many. Agency: National Institutes of Health ($4,754,972; 4/20/15-3/31/19).

6. **Title:** Occurrence of Pesticides in North Carolina Private Drinking Water Wells and Identification of Point-of-Use Treatment Options. PI: Knappe, D.R.U. Co-PIs: LePrevost, C.; de los Reyes, F. Agency: North Carolina Water Resources Research Institute ($120,000; 3/1/18 – 2/28/20).

7. **Title:** Cometabolic Degradation of 1,4-Dioxane in Biologically Active Carbon Filters with Locally Enriched Biota. PI: Knappe, D.R.U (for PhD student Amie McElroy). Agency: North Carolina Water Resources Research Institute ($10,000; 3/1/18 – 2/28/19).

8. **Title:** Design and Application of Cyclodextrin-Based Materials for the Treatment of Legacy and Emerging Perfluoroalkyl Acids. PI: Knappe, D.R.U (for PhD student Zachary Hopkins). Agency: North Carolina Water Resources Research Institute ($10,000; 3/1/18 – 2/28/19).

9. **Title:** EAGER; GOALI: Perfluoroethercarboxylic acids – a new class of drinking water contaminants. PI: Knappe, D.R.U. Agency: National Science Foundation ($89,849; 9/1/15-8/31/16).

10. **Title:** Development of Appropriate Technologies to Treat Drinking Water Co-Contaminants Associated with Chronic Kidney Disease of Unknown Origin. PI: Knappe, D.R.U. Co-PIs: Hoppin, J., Duckworth, O., Polizzotto, M. Agency: NCSU-RISF ($25,000; 1/1/17-12/31/17).

11. **Title:** RAPID; GOALI: Sources of 1,4-Dioxane in the Cape Fear River Watershed of North Carolina and Treatment Options for 1,4-Dioxane Control. PI: Knappe, D.R.U. Agency: National Science Foundation ($50,000; 8/15/14-7/31/15).

12. **Title:** The Effects of Contaminated Soil and Groundwater on Subsurface Utilities, Surface Water and Drainage. PI: Pour-Ghaz, M. Co-PIs: Gabr, M.; Knappe, D.R.U. Agency: NC Dept. of Transportation ($345,381; 8/1/16-7/31/18).

13. **Title:** Generation of Biodegradation - Sorption Barriers for Munitions Constituents. PI: Borden, R.C. Co-PI: Knappe, D.R.U. Agency: US Army Corps of Engineers ($820,000; 3/30/11 – 3/30/16).

14. **Title:** 1,4-Dioxane in North Carolina Drinking Water Sources: Occurrence and Treatment Options. PI: Knappe, D.R.U. Agency: North Carolina Urban Water Consortium ($120,531; 5/15/14 – 5/14/16).

15. **Title:** Evaluation of Flocculants: Optimizing Characteristics and Screening Methods. PI: McLaughlin, R. Co-PI: Knappe, D.R.U. Agency: North Carolina Department of Transportation ($199,523; 8/16/14 – 8/15/16).

16. **Title:** GAC Control of Regulated and Emerging DBPs of Health Concern. PI: Knappe, D.R.U. Agency: Hazen & Sawyer – Prime: Water Research Foundation ($89,998; 2/5/15 – 3/18/17).

17. **Title:** Numerical Modeling of Post-Remediation Impacts of Anaerobic Bioremediation on Groundwater Quality. PI: Borden, R.C. Co-PI: Knappe, D.R.U. Agency: Strategic Environmental Research and Development Program (SERDP) ($506,874; 3/22/11-3/22/15).

18. **Title:** Evaluation of cVOC Removal Efficiencies by Various Technologies. PI: Knappe, D.R.U. Agency: ARCADIS – Prime: Water Research Foundation ($105,000; 10/1/13 – 9/30/15).

19. **Title:** Evaluation of Henry's Law Constant and Freundlich Adsorption Constant for VOCs. PI: Knappe, D.R.U. Agency: Water Research Foundation ($100,000; 10/1/12 – 9/1/15).

20. **Title:** Survey of Existing Volatile Organic Compound (VOC) Treatment Installations. PI: Knappe, D.R.U. Agency: ARCADIS – Prime: Water Research Foundation ($60,000; 10/1/12 – 9/30/14).

21. **Title:** Bromide Occurrence In North Carolina Drinking Water Sources And Effect On Disinfection By-product Formation. PI: Knappe, D.R.U. Agency: North Carolina Water Resources Research Institute and Urban Water Consortium ($87,964; 3/1/13 – 11/28/14).

22. **Title:** New water Treatment Technology Utilizing Non-Thermal Plasma Technology. PI: Shannon, S. (NE, NCSU), co-PI: Knappe, D.R.U. Agency: NCSU Chancellor's Innovation Fund ($72,213; 7/15/13-7/14/14).

23. **Title:** Removal of perfluorinated compounds by powdered activated carbon blends, superfine powdered activated carbon, and magnetic anion exchange resins PI: Knappe, D.R.U. Agency: Water Research Foundation ($150,000; 1/1/11 – 12/31/13).

24. **Title:** Effectiveness of sub-micrometer sized powdered activated carbon for the combined removal of disinfection by-product precursors and trace organic pollutants. PI: Knappe, D.R.U. Agency: Water Research Foundation ($150,000; 10/1/09 – 10/31/12).

25. **Title:** Evaluation of scale-up approaches for the design of GAC contactors. PIs: Summers, R.S. (University of Colorado) and Knappe, D.R.U. Agency: Water Research Foundation ($350,000; 5/1/10 – 10/31/12, NCSU budget is $155,000 plus $20,000 cash contribution from Suffolk County Water Authority).

26. **Title:** Treatment Options for the Removal of Emerging Pollutants of Concern. PI: Knappe, D.R.U. Agency: Urban Water Consortium ($52,919; 1/15/09 – 12/31/10).

27. **Title:** Protecting Receiving Waters: Removal of Biochemically Active Compounds from Wastewater by Ozonation and Activated Carbon Adsorption Processes PI: Knappe, D.R.U. Agency: NC Water Resources Research Institute ($50,000; 3/1/09 – 12/31/10).

28. **Title:** Development of an analytical method for taste and odor compounds and application to NC drinking water sources and finished waters. PI: Knappe, D.R.U. Agency: NC Water Resources Research Institute ($50,000; 3/1/08 – 8/31/09).

29. **Title:** Assessment Landfill Gas Pathway – Laboratory Simulation of Partitioning of Chemical and Biological Contaminants under Anaerobic Decomposition in a Landfill. PI: Barlaz, M. A.; co-PIs: Knappe, D.R.U. and de los Reyes, F.L. Agency: U.S. Environmental Protection Agency ($700,000, 9/1/04 – 12/31/09).

30. **Title:** Decision Support Tool Guidance Document for Management of Debris from Incidents of National Significance. PI: Barlaz, M. A.; co-PIs: Knappe, D.R.U. and de los Reyes, F.L. Agency: Eastern Research Group ($60,282, 9/5/08 – 4/29/09).

31. **Title:** Evaluation of Computational Fluid Dynamics (CFD) for Modeling UV-Initiated Advanced Oxidation Processes. PI: Ducoste, J.; co-PI: Knappe, D.R.U. Agency: American Water Works Association Research Foundation ($150,000; 1/1/06 – 5/15/09).

32. **Title:** Removal of 2-Methylisoborneol and Geosmin with High-Silica Zeolites and Zeolite-Enhanced Ozonation. PI: Knappe, D.R.U. Agency: American Water Works Association Research Foundation ($150,000; 2/1/06 – 5/15/09).

33. **Title:** Impact of UV Location and Sequence on By-Product Formation. PI: Knappe, D.R.U. Agency: NC Water Resources Research Institute Subcontract – primary sponsor is AwwaRF ($21,899; 1/1/08 – 12/31/08).

34. **Title:** Protecting Receiving Waters: Removal of Biochemically Active Compounds from Wastewater by Sequential Photochemical and Biological Oxidation Processes. PI: Knappe, D.R.U. Agency: NC Water Resources Research Institute ($50,000; 3/1/07 – 8/31/08).

35. **Title:** Effect of Prolonged Heating on the Asphalt-Aggregate Bond Strength of HMA Containing Liquid Antistrip Additives. PI: Tayebali, A.A. (NCSU), co-PI, Knappe, D.R.U. Agency: NC Department of Transportation ($163,790; 7/1/06 – 6/30/08).

36. **Title**: High-Silica Zeolites for the Removal of Polar Organic Contaminants from Drinking Water - Development of a 'Green' Adsorption/Regeneration System. PI: Knappe, D.R.U.

Agency: American Water Works Association Research Foundation ($150,000; 2/15/03 – 2/14/06).

37. **Title**: Predicting Single-Solute Adsorption Isotherms for Non-Regulated Contaminants from Fundamental Adsorbent and Adsorbate Properties. PI: Knappe, D.R.U. Agency: U.S. Environmental Protection Agency ($65,000; 8/16/03 – 9/30/06).

38. **Title**: Sequestration Mechanisms and Bioavailability of Tetrachloroethene and Toluene in Solid Waste. Co-PIs: Barlaz, M.A. (NCSU), Knappe, D.R.U. (NCSU) and M. A. Nanny (University of Oklahoma). Agency: National Science Foundation ($566,560; 9/1/01 – 8/31/05). The two co-PIs at NCSU have equal responsibility for this project; University of Oklahoma is a subcontractor.

39. **Title**: Assessment of the Behavior of Chemical and Biological Contaminants in Landfills. PI: Barlaz, M. A. (Knappe, D. R. U. and de los Reyes, F. are also working on this project). Agency: U.S. Environmental Protection Agency. ($100,000, 12/1/03 – 6/30/05).

40. **Title**: Quantifying Anti-Strip Additive in Asphalt (Binders and Mixes). PI: Tayebali, A.A. (NCSU), co-PI, Knappe, D.R.U. Agency: NC Department of Transportation ($111,914; 7/1/03 – 12/31/04).

41. **Title:** Effects of Activated Carbon Surface Chemistry and Pore Structure on the Adsorption of Methyl Tertiary-Butyl Ether and Trichloroethene from Natural Waters. PI: Knappe, D.R.U. Agency: American Water Works Association Research Foundation ($149,985; 1/1/99 – 4/01/02).

42. **Title:** The Effects of Aging and Sorbent Decomposition on the Bioavailability of Toluene and Xylene in Solid Waste. Co-PIs: Barlaz, M.A. (NCSU) and Knappe, D.R.U. Agency: U.S. Environmental Protection Agency ($425,000; 10/1/98 – 3/31/02). The two co-PIs had equal responsibility for this project.

43. **Title:** Optimization of Treatment to Mitigate Impacts of Algae and Algae Control on Finished Water Quality, PI: Knappe, D.R.U., Co-PIs: S. Liehr (NCSU) and J. Burkholder (NCSU). Agency: American Water Works Association Research Foundation and the North Carolina Urban Water Consortium (AWWARF $299,442 plus $24,886 supplement, NC Urban Water Consortium $33,000; in-kind contributions $99,064; 12/1/96 – 5/15/00).

Unsponsored and independent research

1. **Title:** Treatment Strategies for the Combined Removal of VOCs and 1,4-Dioxane from Suffolk County Groundwater (Students: H. Chmielewski and S. Troutman, supported through DHS Fellowship to H.C.), ongoing with S. Ranjithan.

2. **Title:** Advanced Oxidation Technologies for the removal of pharmaceutically active compounds from drinking water (Student: A. Carolina Baeza, supported through an NSF

Graduate Research Fellowship and an NWRI Fellowship), completed Dec. 2009.

3. **Title:** Employing artificial neural networks and genetic algorithms to optimize turbidity and natural organic matter removal in drinking water treatment (Student: A. O. Savas, in collaboration with Dr. S. Ranjithan)

4. **Title**: Adsorption of methyl tertiary-butyl ether on high-silica zeolites (Students: A. Olsson, J. Williams)

5. **Title**: Implementation of an HPLC method to quantify trace levels of hydroxydesethylatrazine in deionized, distilled water and in tap water (Student: G. C. Rucker)

C. Cross-Disciplinary Activities

1. Member of NCSU's Center for Human Health and the Environment. Participated in the development of a time-sensitive R21 proposal that was selected for funding. Currently working on a Superfund Research Center proposal.

2. Successfully developed a collaborative NSF EAGER proposal with Kevin O'Shea in the Department of Chemistry at Florida International University.

3. Member of a team of researchers that developed a successful GRIP proposal entitled "Water Sustainability through Nanotechnology: Nanoscale Science and Engineering at the Solid-Water Interface."

4. Participated in preparation of NSF NRT Proposal "NRT: Resilience of Infrastructure Systems and the Environment (RISE)." (not selected for funding).

5. Member of NCSU Research Network on Water Solutions (ReNeWS).

6. Participated in writing NSF ERC Proposal "RENEE: Resilient Nutrients, Energy, and Environment." Lead: Arizona State University (not selected for funding).

7. Organizer of "Activated Carbon Adsorption" Session at the 2013 AWWA Annual Conference. Denver, CO, June 9-13, 2013.

8. Submitted Chancellor Innovation Fund (CIF) proposal with Dr. S. Shannon (NCSU, Nuclear Engineering). Spring 2012 (not selected for funding), revised and re-submitted in Spring 2013 and selected for funding.

9. Participated in developing a Sustainable Research Networks preproposal that was submitted to NSF. Collaboration between multiple units at NCSU (primarily CCEE and Architecture) and at other universities (US, international). Fall 2011, not selected for funding.

10. Participated in developing a proposal to the Superfund Hazardous Substance Research and Training Program of the National Institute of Environmental Health Sciences (NIEHS). Focus is on health effects associated with trichloroethylene contamination of drinking water at Camp Lejeune. Lead: Jerry LeBlanc, Dept. Head of Environmental & Molecular Toxicology, NCSU (Spring 2010, not selected for funding on first attempt).

11. Developed a joint research proposal with Dr. Howard Weinberg (UNC-CH, ESE) that was selected for funding by the Urban Water Consortium.

12. Gave a presentation about emerging issues and technologies in water and wastewater treatment to the WRRI Advisory Committee, Raleigh, NC, May 13, 2008.

13. Co-organizer of the ACS Symposium "Advances in Adsorption Processes" to be held at the 235th National Meeting & Exposition of the American Chemical Society, New Orleans, LA, April 6-10, 2008.

14. Session co-organizer and invited participant at the NSF-funded Workshop on Models for Sustainable Landfills. March 16-18, 2008, Lewes, DE.

15. Collaborated with Drs. Howard Weinberg (UNC-CH, ESE) and Karl Linden (U. Colorado - Boulder) on a research proposal that was submitted to the American Water Works Association Research Foundation to study disinfection byproduct and assimilable organic carbon formation in UV/H_2O_2 processes. Project was approved for funding and began 1/1/08).

16. IGERT proposal team member (Proposal Title: Globally Engaged Leaders in Innovative Structures & Systems for Climate-Friendly Buildings), Fall 2007

17. Participant at NCSU-EPA Office of Research and Development Meeting to integrate NCSU and EPA research initiatives. April 9, 2007, Research Triangle Park, NC.

18. Invited participant at the NSF-sponsored workshop "Advancing the Quality of Water" to develop future directions in water-quality related research. March 10-12, 2004, Chapel Hill, NC.

19. Collaborated with Dr. Jaap Folmer in the Chemistry Department at NC State University on an NSF-funded project to determine glass transition temperatures for isolated biopolymers and biopolymer composites using differential scanning calorimetry (DSC) to better understand organic contaminant diffusion in municipal solid waste components.

20. Collaborated with Dr. Mark A. Nanny in the School of Civil Engineering & Environmental Science at the University of Oklahoma on an NSF-funded project. Used nuclear magnetic resonance spectroscopy and pyrolysis GC/MS to characterize interactions between xenobiotics and humic substances at the molecular level. In January 2004, a second proposal was submitted with Dr. Nanny, Dr. Morton Barlaz (NCSU, CCEE), and Dr. Neal Blair (NCSU, MEAS) to the biocomplexity program of the National Science Foundation (not

selected for funding).

21. Initiated contact with Dr. JoAnn Burkholder in the Botany Department at NC State University to collaborate on research investigating the removal of algae and algal metabolites from drinking water. Developed a joint proposal that was selected for funding by the American Water Works Association Research Foundation and the Urban Water Consortium.

IV. EXTENSION AND ENGAGEMENT WITH CONSTITUENCIES OUTSIDE THE UNIVERSITY

A. Accomplishments

1. Invited speaker at national and regional workshops, teleconferences, community forums, and other functions
   - Invited panelist at community forums in Wilmington, Brunswick County, and Fayetteville to discuss impacts of GenX on drinking water quality (June 2017 – present)
   - Invited speaker at local seminar series (e.g. Fearrington Village, SAS, 2018)
   - NCAWWA-WEA, Invited Panelist, 2017 Seminar – Wastewater Regulatory Trends and Emerging Issues, Raleigh, NC, June 1, 2017.
   - Chatham Conservation Partners (1,4-dioxane in Pittsboro's drinking water, January 21, 2016).
   - Pittsboro Town Council (1,4-dioxane in Pittsboro's drinking water, September 28, 2015).
   - NC Waterworks Operator Association (hydraulic fracturing, May 6, 2014; UCMR3, August 27, 2014; organics removal, September 23, 2015).
   - Charlotte Water Training Institute, Charlotte, NC, February 5, 2015.
   - Lunch and learn (NCSU, June 5, 2014), West Raleigh Rotary Club (October 17, 2014)
   - Unregulated Data Communications Workshop - Recent North Carolina Research and Associated Data. City of Raleigh, Sept. 16, 2014.
   - Proactive Assessment & Implementation of Future Water Treatment Optimization Goals for Greensboro, Greensboro, NC, May 21, 2014.
   - Bromide Occurrence in the Cape Fear River. Fayetteville Public Utilities Commission, April 10, 2014.
   - Bromide and 1,4-Dioxane in the Cape Fear River Watershed. Triad Area Utilities Meeting, Greensboro, February 5, 2014.
   - AWWA carcinogenic volatile organic contaminants working group. April 30, 2013
   - Triad Area Utilities Meeting. April 11, 2013.
   - NC Public Water Supply Section Disinfection Byproducts Workshop. April 19, 2012.
   - AWWA carcinogenic volatile organic contaminants working group. March 28, 2012.
   - Suffolk County Water Authority, Long Island, NY. June 16, 2011.
   - Hazen & Sawyer Workshop: Emerging Contaminants Research: Implications for Water Treatment, Wastewater Treatment, and Utility Planning. Keynote address. February 17, 2011.
   - NCAWWA-WEA Public Health – Reclaim to Sustain Workshop, March 9, 2010.
   - NC DENR Workshop Public Health & Reclaimed Water, August 27, 2009.
   - Updated NC water utilities on ongoing research in our laboratory. North Carolina Urban Water Consortium Meeting, Charlotte, NC, March 20, 2008.
   - Design Your Own Education Experience (Continuing Education for Practicing Engineers), CCEE Extension Program, Dec. 4, 2007.
   - AWWA Workshop "Advances in the Use of Activated Carbon." Charlotte, NC, November 4, 2007.
   - AWWA Workshop "Advanced Oxidation Technologies in Water Treatment." Charlotte, NC, November 4, 2007.

- Teleconference "Taste & Odor in Drinking Water: Operational Tools and Techniques for Identification and Control." University of North Carolina at Chapel Hill, May 21, 2001.
- Teleconference "Adsorption and Membrane Treatment Technologies: Applications to Water Utilities in North Carolina." University of North Carolina at Chapel Hill, July 24, 1997.

2. Our research on emerging contaminants has been featured by a number of national news services (e.g., PBS News Hour, Washington Post, Chemical & Engineering News, The Intercept) as well as local news outlets (Wilmington Star News, Fayetteville Observer, Carolina Health News, WRAL, WUNC, WHQR). The most impactful article was a June 8, 2017 article by Vaughn Hagerty in the Wilmington Star News, which brought the GenX contamination into the public eye.

3. Assembled stakeholder group consisting of state regulators, drinking water providers, and wastewater discharges to begin to eliminate 1,4-dioxane contamination of drinking water sources in North Carolina. The NCSU research team is meeting regularly with the stakeholder group to provide data updates and to discuss next steps.

4. Our 1,4-dioxane research was featured in an NSF Science Nation video (http://www.nsf.gov/news/special_reports/science_nation/capefearwatershed.jsp). Published May 4, 2015.

5. Provided information to National Public Radio reporter Elizabeth Shogren about 1,4-dioxane occurrence in North Carolina surface water, story aired on March 26, 2014.

6. Taught CE 771 (formerly CE 571) through the Engineering Online program in Fall 1997, Spring 2000, Spring 2002, Spring 2004, Spring 2006, Spring 2008, Spring 2012, Spring 2014, Spring 2016.

7. Taught CE 574 through the Engineering Online program in Fall 2011, Fall 2013, Fall 2015.

B. Program Impacts

Our research on per- and polyfluoroalkyl substances (PFAS) provided the impetus for dramatic decreases in PFAS levels in the drinking water of more than 200,000 residents living in the lower Cape Fear River basin. These improvements resulted in part from voluntary actions by The Chemours company as well as actions mandated by the North Carolina Department of Environmental Quality (DEQ).

As a result of our research on 1,4-dioxane, a working group was formed that includes representatives from DEQ, drinking water providers impacted by 1,4-dioxane, wastewater managers from communities with elevated 1,4-dioxane levels in wastewater, and NCSU researchers. Results of our research informed the working group about the location of 1,4-dioxane discharges and led to the initiation of voluntary source reduction efforts in communities from where 1,4-dioxane originates. In addition, DEQ is considering to revise NPDES discharge permits for municipal wastewater treatment plants in municipalities in

which wastewater contains high levels of 1,4-dioxane. Lowering 1,4-dioxane concentrations in the Cape Fear River watershed is expected to improve the drinking water quality of more than one million North Carolinians.

To maintain licensure, Professional Engineers need to satisfy continuing professional development requirements. By engaging with Professional Engineers at workshops designed to meet continuing professional development requirements, I am able to inform practicing engineers about current research results and technological developments in the water treatment arena. Furthermore, by offering my graduate physico-chemical water treatment course through the Engineering Online program, I am providing opportunities for practicing engineers to further their education.

V. TECHNOLOGICAL AND MANAGERIAL INNOVATION

A. Accomplishments

1. Patent: Very high frequency (VHF) driven atmospheric plasma sources and point of use fertigation of irrigation water utilizing plasma production of nitrogen bearing species. Patent number: 9475710; Inventors: Steven C. Shannon, Detlef Knappe, Brandon Byrns, Daniel Wooten, Alexander Lindsay. October 2016.

2. Collaboration with Hazen and Sawyer, CDM-Smith, Tighe & Bond, and other consulting firms to develop water treatment solutions for PFAS removal.

3. Collaboration with HDR to identify sources of perfluoroalkyl substances in the drinking water supply of the City of Greensboro, NC

4. Collaboration with the Suffolk County Water Authority to assess the effectiveness of granular activated carbon for the removal of perfluoroalkyl substances from ground water

5. Collaboration with Malcolm Pirnie/ARCADIS and the Los Angeles Department of Water and Power to assess treatment options for carcinogenic volatile organic compounds in light of future regulatory scenarios (Spring 2012-present)

6. Research collaborations with drinking water treatment plants across the U.S. (Philadelphia Water Department, Contra Costa Water District, Southern Nevada Water Authority, Central Lake County Joint Action Water Agency, Suffolk County Water Authority, Los Angeles Department of Water and Power, Louisville Water Company, Colorado Springs Utilities, Manatee County Utilities, Kern County Water Authority, and several utilities in North Carolina)

7. Collaboration between the Malcolm Pirnie, Inc. and the University of Colorado, Boulder, to evaluate the effectiveness of activated carbon for the treatment of MTBE-contaminated drinking water wells (Summer 2006, Spring 2007).

8. Prepared reports for AwwaRF that cover such topics as activated carbon selection criteria, algae removal strategies, and MTBE removal strategies.

9. In the Spring 2007 semester, undergraduate and graduate students participated in a study evaluating the effects of switching disinfectants on distribution system water quality for the cities of Raleigh and Cary, NC.

10. I have answered via e-mail and telephone many adsorption- and algae-related questions from water treatment plants and consulting firms across in the US and Canada. I have also provided interested parties with relevant publications of journal articles and conference proceedings.

B. Program Impact

I consider technology transfer an important component of my research and education programs. By engaging with constituencies outside the university, the research results obtained in my research group are being applied by practicing engineers to help improve the quality of drinking water both locally and nationally.

VI. SERVICE TO THE UNIVERSITY AND PROFESSIONAL SOCIETIES

A. Department:

1. Reappointment, Promotion, and Tenure (RPT) Committee Member (Fall 2014 – 2016), Chair (2017 – present).

2. Equipment and Facilities Committee Chair (Fall 2002 – 2012), Equipment and Facilities Committee Member (Fall 1998 – Spring 2002, Fall 2013 - present)
   - Allocated funds among teaching laboratories in the department
   - Prepared annual expenditure reports
   - Prepared "Facilities" section of ABET self-study questionnaire.

3. ABET Assessment Committee for Laboratory Outcomes Member (Fall 2001 - 2015), Chair (Fall 2015 – present)

4. WREE Group Coordinator (Fall 2011 – Spring 2012)

5. Department Head Search Committee member (Spring 2004 – December 2004, Fall 2009 – Spring 2010)

6. Global WaSH Cluster Search Committee member (Fall 2015 – 2018)

7. Awards committee member (Fall 2007 – Spring 2011)

8. EB V/Oval committee member (Fall 2008 – 2010, 2016 – present)

9. Steering committee member for the Department's sustainability task force (Fall 2007 – May 2010)

10. Compact Planning Committee Member (Spring 2007)

11. Search Committee Member for Program Head in Coastal Sustainability and Resilience at the University of North Carolina Coastal Studies Institute (Fall 2007 – Spring 2008)

12. Water Resources and Environmental Engineering Seminar Series Teleconference Coordinator (Fall 1998 - 2004)
    Successfully applied to host distinguished lecturers (AEESP Distinguished Lecturers, Kappe Lecturers) during this time period.

13. Water Resources and Environmental Engineering Faculty Position Search Committees
    Member (Spring 1999)
    Chair (Fall 1997)

14. Open House Committee
    Chair (Fall 1998 – Spring 1999)
    Coordinated Fall 1998 Open House and Spring 1999 Engineering Open House representation of the Civil Engineering Department.
    Member (Fall 1997 - Spring 1998)
    Participant (Spring 1997, Fall 1997, Fall 1999)

15. Flower Fund Chair (Fall 1996 - Summer 1997)

16. Participated in the 2001 "College Welcome"

17. Participated in the Water Resources and Environmental Engineering Spring Symposium (annually starting in Spring 2001)

18. Participated in Air & Waste Management Association Open House (Spring 1998, Spring 1999, Spring 2000)

B. College:

1. Department Representative for Summer Orientation (Spring 1998 – Summer 2000)

2. Occasional guest lecturer for E101 (last in October 2010)

C. NCSU Committees:

1. Technical Advisory Committee member and research advisor for the NCSU Student Chapter of Engineers Without Borders – Advising students, who are working on water supply

projects in Bolivia and Sierra Leone (Fall 2006-present).

2. Faculty Advisor for NC Safewater Student Chapter (2011-present)

3. Mentor for NCSU Global Health Case Competition (April 2010, April 2011).

4. Search committee co-chair for director position of Water Resources Research Institute (March 2008 – March 2009).

5. Mass Spectrometry Users Committee (Spring 1999-2003)

D. State and Regional activities and committee work:

1. NC Science Advisory Board, Member, 2017-present

2. Science Fair Judge at the North Carolina School of Science and Math, Feb. 2012

3. Science Night at Hunter Elementary School. Demonstrated water treatment technologies to K-5 students, April 2010, March 2014.

4. Presented research results from on-line monitoring studies for the detection of algae and bench-scale studies that evaluated the removal of algae from drinking water to members of the North Carolina Urban Water Consortium. February 19, 1998, Greensboro, NC; February 25, 1999, High Point, NC; February 15, 2001, Raleigh, NC. A related presentation was given at a Jordan Lake Stakeholders meeting (January 29, 2004, Greensboro, NC).

5. Provided technical information to the Johnston County Utilities Department (Amanda Bader and Timothy Broome, Smithfield, NC) to improve algae control and treatment strategies (March 2001).

6. Technical review committee member for the expansion/upgrade of the Greenville, NC, water treatment plant.

7. Collaboration with NC water treatment plants on externally funded research projects.

8. Provided technical information to Dave Pritchett of Jamestown Engineering. The information was in regard to the design of an activated carbon adsorption system for the town of Aberdeen, NC, where the pesticide lindane was found in the water supply. Also provided information to the local newspaper on the same topic.

E. National and international activities and committee work:

1. EPA Science Advisory Board, Member, Drinking Water Committee, 2016-present

2. Trustee, AWWA Water Science and Research Division, 2016-present

3. Member, Technical Advisory Council for PFAS Focus Area, The Water Research Foundation, 2017-present.

4. Topic Editor for the Open Access Journal Drinking Water Engineering and Science. January 2011 – present.

5. Associate Editor for Water Science & Technology. March 2009 – February 2013.

6. Member of the Lectures Committee of the Association of Environmental Engineering and Science Professors (AEESP). May 2008 – present. Subcommittee chair for AEESP speaker selection at the AWWA Annual Conference, 2014 – present.

7. Invited member of the American Water Works Association (AWWA) working group for carcinogenic volatile organic compounds. 2011 – 2014.

8. Invited member of the AWWA Publications Award Committee. 2013 – present.

9. External scientific peer reviewer for the State of California Water Resources Control Board Staff Report for "Proposed amendments to statewide water quality control plans for trash." Summer 2014.

10. Co-organizer of the ACS Symposium "Advances in Adsorption Processes" to be held at the 235th National Meeting & Exposition of the American Chemical Society, New Orleans, LA, April 6-10, 2008.

11. Invited member of the American Water Works Association (AWWA) Activated Carbon Standards Committee. The purpose of this committee is to develop and maintain standards and related manuals on adsorptive characteristics of activated carbon for water treatment. June 2003 – present.

    I chaired the Regeneration Standards subcommittee, which was charged with revising AWWA Standard B605 – Standard for Reactivation of Granular Activated Carbon (sent out for balloting in March 2006, revised standard was published by AWWA in 2007).

12. Project Advisory Committee member for the American Water Works Association Research Foundation (AwwaRF). Project Title: Removal of Pesticides and their Degradates by Adsorptive Processes. Peer-review of proposal, project reports and final report. Fall 2006 – Fall 2011. Research team from Technologie-Zentrum Wasser (TZW) in Karlsruhe, Germany.

13. Member of the AWWA Organic Contaminants Research Committee. The purpose of this committee is to assess research results concerning organic contaminant occurrence, behavior, and control in treatment; to point out implications for water supply through seminars and committee reports; and to define research needs. June 2000 – 2005, June 2007 - present.

14. Invited member of the AWWA Particulate Contaminants Research Committee. The purpose of this committee is to identify, evaluate, and communicate research needs, develop ideas for research projects, encourage basic and applied research, and disseminate research results, with a primary focus on particulate contaminants. June 2001 – 2005.

15. Project Advisory Committee member for the American Water Works Association Research Foundation (AWWARF). Project Title: Development of molecular reporters for monitoring *Microcystis* activity and toxicity. Peer-review of project reports and final report. Summer 2001 – 2005. Research team from the University of Tennessee.

16. Project Advisory Committee member for the American Water Works Association Research Foundation (AWWARF). Project Title: Treatability of algal toxins using oxidation, adsorption, and membrane technologies. Peer-review of project reports and final report. Spring 2002 – 2006. Research team: City of Cocoa, FL, and CH2M Hill.

17. Invited Lecturer, Summer School Course on "Presence of Organic Micro-Contaminants in Water: Characterization, Effects And Treatment Alternatives." Environmental Science Doctorate Program, Universidad de Concepcion, Concepcion, Chile, January 4-12, 2010.

18. Invited participant of an international group of researchers to compare experimental and mathematical modeling techniques used to determine the micropore size distribution of carbonaceous adsorbents. October 2002 – 2003.

19. Project Advisory Committee member for AwwaRF. Project Title: The use of oxidants to minimize passage of pathogenic particles through granular media filters. Peer-review of project reports and final report. Summer 2000 – Summer 2003. Research team from Johns Hopkins University.

20. Project Advisory Committee member for AWWARF. Project Title: Characterization of the polar fraction of NOM with respect to DBP formation. Participated in writing of RFP and selection of proposal, peer-review of project reports and final report. Spring 1997 – Spring 2001. Research team members from University of Colorado-Boulder, U.S. Geological Survey, and Metropolitan Water District of Southern California.

21. Peer reviewer for:
    ACS book chapter (Disinfection by-products)
    Adsorption
    AIChE Journal
    Carbon
    Environmental Engineering Science
    Environmental Pollution
    Environmental Science and Technology
    Environmental Science and Technology Letters
    Industrial & Engineering Chemistry Research
    Journal American Water Works Association
    Journal of Colloid and Interface Science
    Journal of Environmental Engineering-ASCE

Journal of Environmental Quality
Journal of Hazardous Materials
Journal of Infrastructure Systems-ASCE
Journal of Material Cycles and Waste Management
Journal of Membrane Science
Journal of Water Supply: Research and Technology-AQUA
Separation Science and Technology
Water Research
Water Science and Technology

I review ~10 manuscripts per year.

22. Peer reviewer for the following funding agencies:
    Water Research Foundation
    Water Reuse Research Foundation
    The Research Council of Norway (2014, 2015)
    National Science Foundation (CAREER panel, CBET Standard Grants Program, Major Research Instrumentation Program)
    U.S. Environmental Protection Agency Grants Program
    U.S. Environmental Protection Agency Graduate Fellowship Program
    U.S. Environmental Protection Agency SBIR Program
    Environmental Research and Education Foundation
    American Chemical Society – Petroleum Research Fund
    US Army Research Office

23. Peer reviewer for the ASCE Environmental Engineering Conference, IWA World Congress, ACS National Meeting.

Exhibit 4

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

SAFER CHEMICALS, HEALTHY FAMILIES et al., *Petitioners,* v. U.S. ENVIRONMENTAL PROTECTION AGENCY et al., *Respondents.* IPC INTERNATIONAL, INC. et al., *Respondents-Intervenors.*	Docket No. 17-72260 Consolidated with Docket Nos. 17-72501, 17-72968, 17-73290, 17-73383, 17-73390

DECLARATION OF VEENA SINGLA, Ph.D.
IN SUPPORT OF PETITIONERS' OPENING BRIEF

I, Veena Singla, declare as follows:

Introduction and Qualifications

1. I am the Associate Director of Science and Policy at the University of California, San Francisco Program on Reproductive Health and the Environment. My research focuses on: indoor environmental quality; understanding exposure pathways for chemicals used in consumer products and building materials; and the mechanisms by which cumulative exposures can lead to adverse health outcomes, especially for vulnerable populations such as workers, pregnant women and young children. The phrase "cumulative exposures" refers to the combination of

exposures to: chemicals during critical windows of development; multiple chemicals; and non-chemical stressors. Through education and communication about relevant research results, I seek to ensure that chemical evaluation methods such as risk assessment and alternatives assessment incorporate current science on exposure pathways, biological susceptibility, the social determinants of health and other relevant fields. I am speaking on behalf of myself in this matter and not as a representative of my employer.

2. I received a Ph.D. from University of California, San Francisco in Developmental and Cellular Biology, and completed a post-doctoral fellowship at Stanford University. My graduate and postdoctoral research focused on how genes control the ways in which cells communicate in vertebrate and invertebrate systems, and the proteins, hormones and small molecules that carry out intra- and inter-cellular signaling. I also studied the developmental origins of disease—the idea that if normal cell signaling during development is disturbed by genetic and/or environmental factors, these perturbations can result in disease and dysfunction later in life.

3. I worked for several years as a Senior Scientist with the Green Science Policy Institute (GSPI), and then served as a Staff Scientist at the Natural Resources Defense Council (NRDC). At GSPI and NRDC, I worked on environmental health science and policy issues relevant to how chemicals in the

environment affect human health. This work included analysis and characterization of flame retardant chemicals in the indoor and built environment, human exposure pathways throughout the chemical lifecycle (i.e., from manufacture, through use and ultimate disposal), and human health hazards. I also completed analysis on the environmental fate, exposure and toxicity properties of the class of halogenated flame retardants which includes hexabromocyclododecane (HBCD), and submitted in-depth scientific and technical comments to the U.S. Environmental Protection Agency (US EPA) on their alternatives assessment evaluation of HBCD.

4. I have extensive experience reviewing data and information from scientific studies and government reports. I have published multiple peer-reviewed articles on the science and policy of flame retardant chemicals in scientific journals. In 2012, I co-authored an article published in Building Research and Information which focused on HBCD.[1]

5. As a recognized expert in the field of human health and the built/indoor environment, I was invited to the first U.S. Green Building Council Summit on Green Building and Human Health in 2012, and to present at a national conference for Occupational and Environmental Medicine Physicians in 2016.

[1] Babrauskas V, Lucas D, Eisenberg D, Singla V, Dedeo M, Blum A. Flame retardants in building insulation: a case for re-evaluating building codes. Build Res Inf. 2012;40(6):738–55.

6. I have presented invited testimony and/or comments on flame retardant chemicals to the US EPA, the Alaska and California legislatures, the Consumer Product Safety Commission, the International Code Council and the San Francisco Board of Supervisors.

7. By virtue of my education, training, and research, and my knowledge of the pertinent scientific literature, I am considered an expert on the sources of human exposure and effects on human health of the flame retardant HBCD. A more complete description of my education and work experience, as well as a complete list of my publications, is attached to this declaration as Exhibit A.

8. The statements in this declaration are scientifically accurate to the best of my knowledge and ability.

Health Hazards of HBCD

9. HBCD is a manmade chemical containing bromine, carbon and hydrogen. US EPA has identified HBCD as one of the first ten chemicals to undergo risk evaluation under the Toxic Substances Control Act (TSCA). EPA's risk evaluation of HBCD covers three related chemicals, which EPA refers to as the "cyclic aliphatic bromides cluster." This cluster of three chemical includes two Chemical Abstract Services Registry Numbers (CASRN) that identify HBCD[2]; and

[2] HBCD is identified by CASRN 3194-55-6 and 25637-99-4. 3194-55-6 is the most accurate CASRN to use for the HBCD technical mixture. However, it has

one CASRN for a substance with no known uses.[3]

10. Much of the information on the toxicity of HBCD comes from studies in laboratory animals. This is so for at least two reasons. First, it is unethical to intentionally expose human subjects to hazardous substances. Second, data from toxicological studies in whole animals, usually rodents, are highly relevant for predicting a chemical's toxicity in humans. For example, every agent that is known to cause cancer in humans is carcinogenic in animals when adequately tested,[4] and almost one-third of human carcinogens were identified after carcinogenic effects were found in well-conducted animal studies.[5] This almost complete concordance across species is seen because animals and humans have the same genetic, metabolic, and systemic processes that affect the biology of disease induction and progression. It is for this reason that animal tests, conducted in accordance with

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historically also been referred to with the CAS RN 25637-99-4, and is referenced with this number in a variety of regulatory documents and authoritative lists.

[3] US EPA (2017) Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Cyclic Aliphatic Bromide Cluster (HBCD).

[4] IARC Monographs Preamble, http://monographs.iarc.fr/ENG/Preamble/.

[5] Huff J. Predicting chemicals causing cancer in animals as human carcinogens. Occup Environ Med. 2010 Oct;67(10):720.

Maronpot RR, Flake G, Huff J. Relevance of animal carcinogenesis findings to human cancer predictions and prevention. Toxicol Pathol. 2004 Mar-Apr;32 Suppl 1:40-8. Review.

Huff J. Chemicals and cancer in humans: first evidence in experimental animals. Environ Health Perspect. 1993 Apr;100:201-10. Review.

strict guidelines for the welfare and use of research animals, are required by regulatory bodies before new pharmaceutical drugs can be tested in humans.[6] In summary, animal experiments provide information on chemical toxicity that is directly applicable to understanding human disease.

11. HBCD causes liver toxicity in animal studies, including increased liver weight, inflammation and accumulation of fat. This liver toxicity occurs when animals are exposed to HBCD as adults or prenatally (before they are born).[7] These kinds of changes are associated with liver damage and disease such as non-alcoholic fatty liver disease, which can lead to cirrhosis and even liver failure.[8]

12. HBCD causes thyroid toxicity in animal studies, and studies in humans reported associations between HBCD exposures and effects on thyroid

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[6] Page R, Baneux P, Vail D, Duda L, Olson P, Anestidou L, Dybdal N, Golab G, Shelton W, Salgaller M, Hardy C. Conduct, Oversight, and Ethical Considerations of Clinical Trials in Companion Animals with Cancer: Report of a Workshop on Best Practice Recommendations. J Vet Intern Med. 2016 Mar-Apr;30(2):527-35.

Workman P, Aboagye EO, Balkwill F, Balmain A, Bruder G, Chaplin DJ, Double JA, Everitt J, Farningham DA, Glennie MJ, Kelland LR, Robinson V, Stratford IJ, Tozer GM, Watson S, Wedge SR, Eccles SA; Committee of the National Cancer Research Institute. Guidelines for the welfare and use of animals in cancer research. Br J Cancer. 2010 May 25;102(11):1555-77.

[7] US EPA (2017). Scope of the Risk Evaluation for Cyclic Aliphatic Bromides Cluster (hereinafter, "EPA HBCD Scope Document").

[8] Kim, W., 2002. Burden of liver disease in the United States: Summary of a workshop. Hepatology, 36(1), pp.227–242. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12085369.

hormones.[9] Normal thyroid hormone levels and function, especially during the prenatal period, are essential for healthy brain development. Prenatal exposures to chemicals that cause thyroid toxicity can, in effect, scramble thyroid hormone signals, leading to abnormal brain development and health impacts such as loss of cognitive capacity/IQ, attention, learning, memory and motor or coordination problems.[10] In adults, thyroid hormones help maintain normal physiology and metabolism. Perturbations can lead to hyper- or hypo-thyroid disease.

13. HBCD causes neurotoxicity to the developing brain in animal studies. HBCD exposures in young animals caused changes in movement and brain function, and these effects persisted into adulthood. It is believed that thyroid toxicity may be one mechanism by which HBCD causes these effects. HBCD exposure also caused changes in hearing and the functioning of the critical neurotransmitter dopamine.[11] Dopamine is involved in brain processes including response to reward and addiction.

14. HBCD causes reproductive toxicity in animal studies, with reduced fertility and fewer successful pregnancies seen in females.[12]

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[9] EPA HBCD Scope.

[10] Zoeller TR. Environmental chemicals targeting thyroid. Horm. 2010;9(1):28–40.

[11] EPA HBCD Scope Document.

[12] EPA HBCD Scope Document.

15. As stated above, the results of these animal toxicology studies indicate HBCD's toxicity to humans. According to US EPA, HBCD "can reasonably be anticipated to cause developmental and reproductive effects in humans and is highly toxic to aquatic and terrestrial organisms."[13] These health hazards are especially of concern for women of reproductive age, fetuses, infants and young children because the developing reproductive and nervous system is particularly vulnerable to disruption by toxic chemicals.[14] Just as low-level lead exposures that would not harm an adult can be highly poisonous to a child, HBCD exposures during critical windows of a child's brain and reproductive system development

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[13] 81 FR 85440 Nov 28, 2016. Addition of Hexabromocyclododecane (HBCD) Category; Community Right-to-Know Toxic Chemical Release Reporting.

[14] Grandjean P, Bellinger D, Bergman A, Cordier S, Davey- Smith G, Eskenazi B, et al. The Faroes statement: human health effects of developmental exposure to chemicals in our environment. Basic Clin Pharmacol Toxicol 2008;102:73–5.

Crain DA, Janssen SJ, Edwards TM, Heindel J, Ho SM, Hunt P, et al. Female reproductive disorders: the roles of endocrine-disrupting compounds and developmental timing. Fertil Steril 2008;90:911–40.

Diamanti-Kandarakis E, Bourguignon J-P, Giudice LC, Hauser R, Prins GS, Soto AM, et al. Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. Endocr Rev. 2009 Jun;30(4):293–342.

Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, Prins GS, et al. EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals. Endocr Rev. 2015 Dec;36(6):E1–150.

Bennett D, Bellinger DC, Birnbaum LS, Bradman A, Chen A, Cory-Slechta DA, et al. Project TENDR: Targeting Environmental Neuro-Developmental Risks The TENDR Consensus Statement. Environ Health Perspect. 2016 Jul 1;124(7).

can be toxic to this susceptible population at levels that may not harm other populations.

HBCD is a Persistent, Bioaccumulative and Toxic Chemical

16. According to US EPA, "[B]ased on the available bioaccumulation and persistence data, EPA has determined that HBCD should be classified as a persistent, bioaccumulative, and toxic (PBT) chemical…"[15] Persistence in the environment means that HBCD does not break down after it is released into the environment. Bioaccumulation means that HBCD builds up in wildlife and people, accumulating to higher and higher levels in the body as it moves up the food chain. Because HBCD is harmful to the health of living organisms, as described above, it is considered toxic.

17. HBCD is designated as a persistent, bioaccumulative and toxic chemical (also knowns as a PBT or POP, persistent organic pollutant) by the Stockholm Convention[16] and US EPA's Toxics Release Inventory.[17]

Sources and Uses of HBCD

[15] 81 FR 85440 Addition of Hexabromocyclododecane (HBCD) Category; Community Right-to-Know Toxic Chemical Release Reporting.

[16] Stockholm Convention. SC-6/13: Listing of hexabromocyclododecane

[17] 81 FR 85440 Addition of Hexabromocyclododecane (HBCD) Category; Community Right-to-Know Toxic Chemical Release Reporting

18. The total volume of HBCD manufactured or imported in the U.S. in 2015 was between 1 and 10 million pounds. It is added as a flame retardant to building materials, electronics, floor coverings, furniture, and fabrics.[18]

19. The major use of HBCD (90% of production volume) is in building insulation, specifically expanded and extruded polystyrene materials.[19] Existing buildings in the U.S. contain 66-132 million pounds of HBCD.[20]

20. HBCD is a semi-volatile organic chemical which is also used additively in plastic materials and on textiles. For example, HBCD is added to plastic cases (high-impact polystyrene (HIPS)) used for televisions, computers, printers and other electronics; and as a coating on fabrics including furniture upholstery and curtains.[21]

21. HBCD can migrate out of products and partition into air and dust in

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[18] EPA HBCD Scope Document.

[19] Babrauskas V, Lucas D, Eisenberg D, Singla V, Dedeo M, Blum A. Flame retardants in building insulation: a case for re-evaluating building codes. Build Res Inf. 2012;40(6):738–55.

EPA HBCD Scope Document.

[20] Safer Chemicals, Healthy Families et al. Comments to the U.S. Environmental Protection Agency (EPA) on the Scope of its Risk Evaluation for the TSCA Work Plan Chemicals: CYCLIC ALIPHATIC BROMIDE CLUSTER or HEXABROMOCYCLODODECANE (HBCD). March 15, 2017. https://healthybuilding.net/uploads/files/saferchemicals-hbcd.pdf

[21] Stubbings WA, Harrad S. Extent and mechanisms of brominated flame retardant emissions from waste soft furnishings and fabrics: A critical review. Environ Int. 2014 Oct;71:164–75.

the occupied spaces of buildings.[22] HBCD is found in the dust of homes, commercial buildings, vehicles, airplanes, schools, daycares and college dormitories.[23]

22. HBCD is released to air, water, and land during the chemical's manufacture, processing, and use in products, as well as with the recycling and disposal of such products.[24] Environmental monitoring studies find significantly

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[22] Weschler, C.J. & Nazaroff, W.W., 2008. Semivolatile organic compounds in indoor environments. Atmospheric Environment, 42(40), pp.9018–9040.

Rauert C, Lazarov B, Harrad S, Covaci A, Stranger M. A review of chamber experiments for determining specific emission rates and investigating migration pathways of flame retardants. Atmos Environ. 2014;82:44–55.

[23] US EPA, 2015. TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Cyclic Aliphatic Bromides Cluster Flame Retardants. Office of Chemical Safety and Pollution Prevention, EPA Document# 743-D1-5001, pg. 26

Harrad, S. et al., 2010. Dust from U.K. primary school classrooms and daycare centers: The significance of dust as a pathway of exposure of young U.K. children to brominated flame retardants and polychlorinated biphenyls. Environmental Science and Technology, 44(11), pp.4198–4202.

Harrad, S. & Abdallah, M.A.-E., 2011. Brominated flame retardants in dust from UK cars – Within-vehicle spatial variability, evidence for degradation and exposure implications. Chemosphere, 82(9), pp.1240–1245.

Dodson RE, Rodgers KM, Carey G, Cedeno Laurent JG, Covaci A, Poma G, et al. Flame Retardant Chemicals in College Dormitories: Flammability Standards Influence Dust Concentrations. Environ Sci Technol. 2017 Apr 13;acs.est.7b00429.

Mitro SD, Dodson RE, Singla V, Adamkiewicz G, Elmi AF, Tilly MK, et al. Consumer Product Chemicals in Indoor Dust: A Quantitative Meta-analysis of U.S. Studies. Environ Sci Technol. 2016;acs.est.6b02023.

[24] EPA HBCD Scope Document.

higher levels of HBCD in the air, water, sediment, soil and animals near facilities that manufacture, process (including recycling) and dispose of HBCD and/or products containing HBCD.[25]

23. Because HBCD is persistent in the environment, it is subject to long-range transport and is found in the air of urban and remote environments; surface and ocean water; soil, sediment and sewage sludge; in marine and freshwater fish; and in animals including marine mammals, birds and their eggs.[26]

24. Environmental releases result in contamination of food with HBCD. HBCD is found in peanut butter, fish, poultry and pork products purchased at U.S. grocery stores.[27] HBCD also contaminates traditional foods such as wild fish and

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[25] Covaci A, Gerecke AC, Law RJ, Voorspoels S, Kohler M, Heeb N V, et al. Hexabromocyclododecanes (HBCDs) in the environment and humans: A review. Environ Sci Technol. 2006 Jun;40(12):3679–88.

Zhu H, Zhang K, Sun H, Wang F, Yao Y. Spatial and temporal distributions of hexabromocyclododecanes in the vicinity of an expanded polystyrene material manufacturing plant in Tianjin, China. Environ Pollut. 2017 Mar;222:338–47.

Stubbings WA, Harrad S. Extent and mechanisms of brominated flame retardant emissions from waste soft furnishings and fabrics: A critical review. Environ Int. 2014 Oct;71:164–75.

[26] Law RJ, Covaci A, Harrad S, Herzke D, Abdallah MA-E, Fernie K, et al. Levels and trends of PBDEs and HBCDs in the global environment: Status at the end of 2012. Environ Int. 2014 Apr;65:147–58.

Stockholm Convention Persistent Organic Pollutants Review Committee. (2010) Risk profile on hexabromocyclododecane. UNEP/POPS/POPRC.6/13/Add.2

[27] Schecter A, Szabo DT, Miller J, Gent TL, Malik-Bass N, Petersen M, et al. Hexabromocyclododecane (HBCD) Stereoisomers in U.S. Food from Dallas, Texas. Environ Health Perspect. 2012 May 31;120(9):1260–4.

marine mammals relied on by arctic, indigenous and other communities for some portion of their diets.[28]

Human Exposure to HBCD

25. Because HBCD is not bound to the materials to which it is added and because it is semi-volatile, HBCD migrates out of products into indoor air and dust.[29] It can migrate in three ways: (1) as a vapor or gas, with subsequent inevitable attachment to house dust; (2) physical abrasion of particles from the treated product directly into dust; and (3) direct contact between the surface of the treated product and dust.[30]

Schecter A, Haffner D, Colacino J, Patel K, Päpke O, Opel M, et al. Polybrominated diphenyl ethers (PBDEs) and hexabromocyclodecane (HBCD) in composite U.S. food samples. Environ Health Perspect. 2010 Mar;118(3):357–62.

[28] de Wit CA, Herzke D, Vorkamp K. Brominated flame retardants in the Arctic environment - trends and new candidates. Sci Total Environ. 2010;408(15):2885–918.

Arctic Monitoring and Assessment Program. (2016) AMAP Assessment 2016: Chemicals of Emerging Arctic Concern.

Suk WA, Avakian MD, Carpenter D, Groopman JD, Scammell M, Wild CP. Human exposure monitoring and evaluation in the Arctic: The importance of understanding exposures to the development of public health policy. Environ Health Perspect. 2004;112(2):113–20.

[29] EPA HBCD Scope Document.

[30] Rauert C, Lazarov B, Harrad S, Covaci A, Stranger M. A review of chamber experiments for determining specific emission rates and investigating migration pathways of flame retardants. Atmos Environ. 2014;82:44–55.

Rauert C, Kuribara I, Kataoka T, Wada T, Kajiwara N, Suzuki G, et al. Direct contact between dust and HBCD-treated fabrics is an important pathway of source-to-dust transfer. Sci Total Environ. 2016 Mar;545–546:77–83.

26. This HBCD-contaminated dust moves away from treated products through the air and settles down, coating the surface of floors, carpets and indoor objects. Studies find ubiquitous HBCD contamination of indoor environments including cars, homes, schools, and other buildings; across studies, HBCD is detected in 92-100% of indoor dust samples.[31] Because people spend more than 90% of their time indoors in the U.S.,[32] indoor exposures are particularly important for the general population.

27. HBCD enters the bodies of adults and children in the general population when people: breathe in contaminated air; touch products containing HBCD or put such products in their mouths; touch, breathe in, or accidentally ingest contaminated indoor dust; drink contaminated water; and eat contaminated food.

28. Young children who crawl, play on the floor, and put their hands in their mouths have greater exposure to contaminated indoor dust compared to adults, and their exposure to HBCD via dust would be elevated.[33] HBCD also

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[31] Mitro SD, Dodson RE, Singla V, Adamkiewicz G, Elmi AF, Tilly MK, et al. Consumer Product Chemicals in Indoor Dust: A Quantitative Meta-analysis of U.S. Studies. Environ Sci Technol. 2016;acs.est.6b02023.

[32] Klepeis, N. E.; Nelson, W. C.; Ott, W. R.; Robinson, J. P.; Tsang, A.M.; Switzer, P.; Behar, J. V.; Hern, S. C.; Engelmann, W. H. The National Human Activity Pattern Survey (NHAPS): a resource for assessing exposure to environmental pollutants. J. Exposure Anal. Environ. Epidemiol. 2001, 11 (3), 231–252.

[33] US EPA. Exposure Factors Handbook.

contaminates breastmilk, and diet is the major source of HBCD exposure for infants.[34, 35] Further, recent testing found HBCD in children's car seats,[36] and data indicates that baby products are an important contributor to children's exposure for other flame retardants.[37] Children have 3-15 times higher levels of exposure to other kinds of flame retardant chemicals compared to adults; because the exposure pathways are similar, children are also at risk for higher exposures to HBCD.[38]

29. Subsistence populations rely on natural resources to provide some portion of their diet. These populations, including many indigenous communities, consume significantly more and different types of fish compared to the general

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[34] EPA HBCD Scope Document.

[35] Fromme H, Becher G, Hilger B, Völkel W. Brominated flame retardants – Exposure and risk assessment for the general population. Int J Hyg Environ Health. 2015;219(1):1–23.

[36] Ecology Center 2016. Children's Car Seat Study 2016- Report. Available: http://www.ecocenter.org/healthy-stuff/pages/childrens-car-seat-study-2016-report

[37] Hoffman K, Butt CM, Chen A, Limkakeng AT, Stapleton HM. High Exposure to Organophosphate Flame Retardants in Infants: Associations with Baby Products. Environ Sci Technol. 2015 Dec 15;49(24):14554–9.

[38] Lunder S, Hovander L, Athanassiadis I, Bergman Å. Significantly Higher Polybrominated Diphenyl Ether Levels in Young U.S. Children than in Their Mothers. Environ Sci Technol. 2010 Jul 1;44(13):5256–62.

Butt CM, Congleton J, Hoffman K, Fang M, Stapleton HM. Metabolites of Organophosphate Flame Retardants and 2-Ethylhexyl Tetrabromobenzoate in Urine from Paired Mothers and Toddlers. Environ Sci Technol. 2014 Sep 2;48(17):10432–8.

population, and thus their exposures to HBCD via diet would be elevated.[39]

30. The environmental monitoring studies cited above find significantly higher levels of HBCD in the air, water, sediment, soil and animals near facilities that historically or currently produce, process, recycle or dispose HBCD or HBCD-containing products. Given these higher levels, it is likely that communities near such facilities would have elevated exposures to HBCD. Because HBCD is persistent in the environment, HBCD levels around such facilities would be expected to remain elevated even if the facility no longer produces or processes HBCD.

31. Because HBCD is persistent and bioaccumulative, environmental releases will manifest in continued contamination of water, crops, livestock and wild foods.[40] These sources will result in ongoing human exposures, likely for many decades into the future. Evidence from other persistent and bioaccumulative chemicals demonstrates that after production bans, human exposure initially

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[39] US EPA. Exposure Factors Handbook, Chapter 10: Intake of Fish and Shellfish.

Suk WA, Avakian MD, Carpenter D, Groopman JD, Scammell M, Wild CP. Human exposure monitoring and evaluation in the Arctic: The importance of understanding exposures to the development of public health policy. Environ Health Perspect. 2004;112(2):113–20.

[40] Harrad S, Diamond ML. New Directions: Exposure to polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs): Current and future scenarios. Atmos Environ. 2006 Feb;40(6):1187–8.

declines, but then remains steady because of ongoing exposures from existing products, diet, etc.[41]

32. Workers who manufacture or process HBCD, or handle HBCD-containing products such as building materials, would have additional sources of HBCD exposure through skin contact and inhalation of contaminated air and dust. As buildings with HBCD-containing insulation are remodeled, rehabilitated and demolished, existing insulation that is recycled or landfilled will lead to worker exposures and environmental contamination.[42] For example, a 2012 study in Environmental Science and Technology found that cutting building insulation boards releases microscopic particles containing HBCD that could be inhaled deep into the lung.[43] Furniture, electronics and other products containing HBCD will

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[41] Zota AR, Linderholm L, Park J-S, Petreas M, Guo T, Privalsky ML, et al. Temporal Comparison of PBDEs, OH-PBDEs, PCBs, and OH-PCBs in the Serum of Second Trimester Pregnant Women Recruited from San Francisco General Hospital, California. Environ Sci Technol. 2013 Oct 15;47(20):11776–84.

Parry E, Zota AR, Park J-S, Woodruff TJ. Polybrominated diphenyl ethers (PBDEs) and hydroxylated PBDE metabolites (OH-PBDEs): A six-year temporal trend in Northern California pregnant women. Chemosphere. 2018;195:777–83.

[42] Babrauskas V, Lucas D, Eisenberg D, Singla V, Dedeo M, Blum A. Flame retardants in building insulation: a case for re-evaluating building codes. Build Res Inf. 2012;40(6):738–55.

[43] Zhang H, Kuo Y-Y, Gerecke AC, Wang J. Co-release of hexabromocyclododecane (HBCD) and Nano- and microparticles from thermal cutting of polystyrene foams. Environ Sci Technol. 2012 Oct;46(20):10990–6.

also contribute to worker exposures and environmental contamination as they are recycled and disposed.[44] In this way, workers may be exposed to HBCD through their handling of HBCD-containing products at the end of the products' life. Additionally, workers would have elevated exposures to HBCD because on-the-job exposures occur in addition to the HBCD exposures they experience at home and via diet, etc., that are also experienced by the general population.

Risks from Aggregate and Cumulative Exposures

33. In general, the equation ***Hazard x Exposure = Risk*** is a simplified representation of the risk assessment calculation. In US EPA's risk evaluation of HBCD under the Toxic Substances Control Act, HBCD's health hazards will be considered in conjunction with the dose, or exposure, of HBCD received into the body to calculate the total health risk presented by HBCD. Therefore, if the hazard or the exposure is understated, then the risk will be understated.

34. It is not possible to determine, *a priori*, which use(s) of a chemical carry the highest risk(s) without a comprehensive examination of the chemical's hazards and exposures. For example, the volume of a chemical put into a particular use is often used as a surrogate to estimate potential exposure—the higher-volume the use, the higher the potential exposure. But this simplistic assumption does not

[44] Stubbings WA, Harrad S. Extent and mechanisms of brominated flame retardant emissions from waste soft furnishings and fabrics: A critical review. Environ Int. 2014 Oct;71:164–75.

always hold true. In the case of HBCD, 90% of the production volume is used in building insulation, and 10% of production volume is used in other applications including electronics cases and textiles. The simplistic assumption would be that building insulation uses contribute most to human exposures for the general population. But if we consider indoor HBCD exposures, data shows that actually, furniture and electronics contribute significantly to indoor levels of HBCD through the migration pathways described above.[45] Specifically, HBCD levels in dust were significantly higher: near a television containing HBCD compared to other areas in a room;[46] and in college dormitories adhering to stricter flammability standards that result in more furniture being treated with flame retardants, including HBCD.[47] In fact, the highest levels of HBCD ever measured in indoor dust in the U.S. were found in college dormitories, an exposure that would not be accounted

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[45] Rauert C, Lazarov B, Harrad S, Covaci A, Stranger M. A review of chamber experiments for determining specific emission rates and investigating migration pathways of flame retardants. Atmos Environ. 2014;82:44–55.

Rauert C, Kuribara I, Kataoka T, Wada T, Kajiwara N, Suzuki G, et al. Direct contact between dust and HBCD-treated fabrics is an important pathway of source-to-dust transfer. Sci Total Environ. 2016 Mar;545–546:77–83.

[46] Harrad S, Abdallah MAE, Covaci A. Causes of variability in concentrations and diastereomer patterns of hexabromocyclododecanes in indoor dust. Environ Int. 2009 Apr;35(3):573–9.

[47] Dodson RE, Rodgers KM, Carey G, Cedeno Laurent JG, Covaci A, Poma G, et al. Flame Retardant Chemicals in College Dormitories: Flammability Standards Influence Dust Concentrations. Environ Sci Technol. 2017 Apr 13;acs.est.7b00429.

for if only exposures from the highest volume use were considered.

35. HBCD enters people's bodies from many sources including indoor and outdoor environments, products, water and food. All of these sources contribute to the total dose, or exposure, of HBCD in the body. Excluding any known source of exposure—for example from food—will underestimate total exposure, and thus underestimate the total risk of HBCD.

36. Exposures can be also underestimated by failing to consider the actual duration of the exposure. For example, children would experience almost continuous HBCD exposure throughout the day as they move between home, cars and school or daycare. Assuming children are exposed to HBCD only 8 hours a day would underestimate their exposure and underestimate risk. Further, multiple exposure spikes over time (known as "repeated dose" exposures) can have a sensitizing effect, resulting in a more severe reaction to a second, third or fourth exposure than occurred to the first. If the effects of multiple exposures are not considered, risk would be underestimated.

37. Underestimation of exposure is especially consequential for the sub-populations of women of reproductive age, fetuses, infants and young children who have greater biological susceptibility to HBCD toxicity, and thus could experience harm at lower levels of HBCD exposure than other populations.

Conclusion

38. HBCD is a persistent, bioaccumulative and toxic chemical that presents threats to human and environmental health. A person's risk of suffering harm from exposure to HBCD depends on the totality of a person's exposures from all sources, including from existing products *in situ* in buildings and disposal of such products. If EPA fails to account for all sources and uses, risk to populations including workers, communities, subsistence populations, women, fetuses, infants and children would be underestimated. In that case, one or more of these populations could suffer health harms as a result of HBCD exposures, including but not limited to liver damage, infertility, decreased IQ, and attention problems.

I declare under penalty of perjury that the foregoing is true and correct.

Executed on April 3, 2018.

Veena Singla

Exhibit A

to the Declaration of Veena Singla, Ph.D.
in Support of Petitioners' Opening Brief

VEENA SINGLA, PH.D.

120 Wetmore St. #5
San Francisco, CA 94108

(469) 236-5549
veena.singla@gmail.com

EDUCATION

From	To	Institution	Degree	Major	PhD Advisor
08/1997	05/2001	University of California, Berkeley	B.S.	Chemistry	
09/2003	09/2010	University of California, San Francisco	PhD	Cell Biology	Jeremy Reiter
04/2011	05/2012	Stanford University	Postdoctoral Fellowship		

OTHER POSITIONS

From	To	Institution	Position	Department
09/2008	12/2011	University of San Francisco	Adjunct Professor	Biology
04/2010	08/2010	KQED Public Media for Northern California	Education Intern	QUEST
05/2012	10/2013	Green Science Policy Institute	Senior Scientist	
01/2014	6/2017	Natural Resources Defense Council (NRDC)	Staff Scientist	Health and Environment Program

HONORS AND AWARDS

Year	Name	Organization
2001	High honors (Summa cum laude)	UC Berkeley Chemistry Department
2004	Graduate Research Fellowship	National Science Foundation
2006	Richard Fineberg Memorial Teaching Award	UC San Francisco
2008	Scholarship recipient	Phi Beta Kappa Association of Northern California
2009	Outstanding poster presentation	California Academy of Sciences Evolution Symposium

PROFESSIONAL ORGANIZATIONS

From	To	Organization
07/2014	Present	American Chemical Society

SERVICE TO PROFESSIONAL ORGANIZATIONS

From	To	Organization	Role
01/2013	Present	Californians for Toxic-Free Fire Safety Coalition	Co-lead

09/2014	Present	Healthy Babies, Bright Futures Integrated Flame Retardant Campaign	Steering Committee member

INVITED PRESENTATIONS

Category	Year	Organization	Role	Type
International	2007	FASEB Biology of Cilia and Flagella International Meeting	Speaker	Podium
Regional	2011	Green Campus Energy Efficiency Summit	Speaker	Podium
National	2014	14th Annual Workshop on Brominated and Other Flame Retardants	Speaker	Podium
National	2014	Green Chemistry Clearinghouse	Speaker	Panel
National	2014	American Chemical Society National Meeting	Speaker	Panel
National	2014	Health and Environmental Funders Network meeting	Speaker	Panel
National	2015	Green Chemistry Clearinghouse	Speaker	Panel
National	2015	SXSW Eco	Speaker	Panel
Other	2016	UCSF Grand Rounds	Speaker	Podium
National	2016	Toxic Substances in the Workplace and the Environment Conference	Speaker	Podium
Regional	2016	Environmental Chemistry Laboratory Seminar Series, California Department of Toxic Substances Control	Speaker	Podium
National	2016	Society of Environmental Journalists Annual Conference	Speaker	Panel

PROFESSIONAL DEVELOPMENT ACTIVITIES

UCSF Becoming an Effective Science Teacher (BEST) and Teaching Apprenticeship Program (TAP) courses

SERVICE ACTIVITIES SUMMARY

My service activities have focused on providing career development mentorship for graduate students interested in science policy and communication.

Category	From	To	Organization	Role
UCSF Campuswide	04/2010	04/2011	UCSF Green Campus (Alliance to Save Energy)	Team leader
Other University	2011	2011	Stanford Splash! Education Program	Class leader
UCSF Campuswide	09/2010	2014	UCSF Graduate Student Internships for Career Exploration	Alumnus advisor- Participate in roundtables/ panels at bi-annual events
UCSF Campuswide	09/2014	Present	UCSF Motivating INformed Decisions (MIND) Program	Mentor (conduct about 1 informational interview/ month)

COMMUNITY AND PUBLIC SERVICE

From	To	Organization	Role
1999	2001	UC Berkeley Disabled Students Program	Tutor
1999	2001	South Berkeley YMCA	Volunteer
2008	2009	Golden Gate Parks Conservancy	Volunteer
2011	2011	California Academy of Sciences	Volunteer

CONTRIBUTIONS TO DIVERSITY

As manager of NRDC's internship program, I expanded our recruitment efforts to include more diverse Bay Area schools such as Touro University and University of San Francisco (USF), both majority minority institutions. I have guest lectured at Touro every year since 2013 and we hosted our first USF intern in 2017.

TEACHING SUMMARY

I am an experienced educator with significant curriculum development, evaluation and teaching experience. I use an evidence-based approach to teaching drawing from research in science education, cognitive science and psychology. I have experience working with diverse student populations, including minority, low-income and disabled.

FORMAL TEACHING

University	Year	Class	Department	Role
UCSF	2004-05	Biochemistry Fundamentals and Cancer Block	Medical School	Teaching assistant
University of San Francisco	2008	Introductory Biology	Biology	Laboratory teaching assistant
University of San Francisco	2009	Advanced Genetics	Biology	Lecturer and curriculum development
University of San Francisco	2010	"The Science of Life" Biology for non-majors	Biology	Lecturer and Laboratory Instructor, curriculum development
Stanford University	2011-12	Core Molecular Biology Laboratory (Bio 44X)	Biology	Laboratory instructor, curriculum development, and evaluation

MENTORING SUMMARY

I have served as the primary mentor for undergraduate, master's, and pre-doctoral students as well as physician fellows in internships ranging from 1 month- 1 year.

Student	Year	Current Position	Mentor Type	Role
Nichole Johnston (Undergraduate intern)	2013	Graduate student, Biochemistry, Yale University	Research, project, career mentor	Full-time mentor, 3 months, meetings once a week

Student	Year	Current Position	Mentor Type	Role
Biruk Tammru (MPH candidate)	2014	Design Researcher at Gobee Group	Research, project, career mentor	Full-time mentor, 3 months, meetings once a week
Raj Puri (MD fellow)	2014		Project mentor	Full-time mentor, 1 month, meetings once a week
Jacqueline Levere (Undergraduate intern)	2014		Research, project, career mentor	Full-time mentor, 3 months, meetings once a week
Lee Ann Hill	2015	Associate, Environmental Health at PSE Healthy Energy	Research, project, career mentor	Full-time mentor, 3 months, meetings once a week
Yi Krystal Lin (MD fellow)	2015	Physician, The Permanente Medical Group	Research and project mentor	Full-time mentor, 1 month, meetings once a week
Anna Reade (predoctoral student)	2016	Senate Fellow, California Council on Science and Technology	Research, project, career mentor	Full-time mentor, 3 months, meetings once a week
Shuchi Aggarwal (MD fellow)	2016	Resident Physician in Occupational and Environmental Medicine at UCSF	Project mentor	Full-time mentor, 1 month, meetings once a week
Alex Shi (MPH candidate)	2016		Research, project, career mentor	Full-time mentor, 3 months, meetings once a week
Lucia Ruiz (MPH candidate)	2017		Research, project, career mentor	Full-time mentor, 3 months, meetings once a week
Monica Kaitz (MD fellow)	2016-17		Research and project mentor	Meetings once a month; one publication completed and another in progress

RESEARCH AND CREATIVE ACTIVITIES SUMMARY

I have developed, secured funding for, and managed strategic new research initiatives on chemical exposures in the indoor environment and vulnerable populations. These include multiple collaborative, interdisciplinary research projects at the intersection of environmental health and policy.

At Green Science Policy Institute, I led a multi-disciplinary team of fire scientists (from Lawrence Berkeley National Laboratory and industry) and environmental health and policy experts (from UC Berkeley and non-governmental organizations (NGOs)) to publish the first-of-its-kind paper on flammability standards, building codes and toxic chemicals in the built environment.

Recently, I led a team of seven scientists investigating consumer product chemicals in the indoor environment, bringing together academic, NGO, and medical researchers from George Washington University, Silent Spring Institute, Harvard School of Public Health and UCSF. I provided the vision and funding for the project, resulting in a publication in a leading journal and extensive media coverage.

RESEARCH AWARDS

Category	Role	Funding Source	Date	Total Direct Costs	Project Description
Past	Project lead	NRDC Science Center	2015-16	$50,000	A quantitative meta-analysis of consumer product chemicals in U.S. indoor dust
Past	Project co-lead	Healthy Babies, Bright Futures	2015	$10,000	Risk assessment of flame retardant chemical clusters
Past	Project co-lead	Ziering Family Foundation	2015	$10,000	Risks of the pesticide chlorpyrifos
Past	Project co-lead	Healthy Babies, Bright Futures	2016	$15,000	Evaluation of flame retardant chemical data
Current	Project co-lead	Healthy Babies, Bright Futures	2017	$15,000	Evaluation of flame retardant chemical data

PEER-REVIEWED PUBLICATIONS

1. Corbit, K.C., Aanstad, P., **Singla, V.**, Norman, A.R., Stainier, D.Y., Reiter, J.F. (2005) Vertebrate Smoothened functions at the primary cilium. *Nature*. 437 (7061): 1018-1021
2. **Singla, V.** and Reiter, J.F. (2006) The primary cilium as the cell's antenna: signaling at a sensory organelle. *Science*. 313 (5787): 629-633
3. **Singla, V.**, Hunkapiller, J., Santos, N., Seol, A.D., Norman, A.R., Wakenight, P., Skarnes, W.C., Reiter, J.F. (2010) Floxin, a resource for genetically engineering mouse ESCs. *Nature Methods*. Jan;7(1):50-2.
4. **Singla, V.**, Romaguera-Ros, M., Garcia-Verdugo, J.M., Reiter, J.F. *Ofd1*, a human disease gene, regulates the length and distal structure of centrioles. (2010) *Developmental Cell* Mar 16; 18(3): 410-424.
5. Hunkapiller, J., **Singla, V.**, Seol, A.D., Reiter, J.F. (2011) The ciliogenic protein Oral-Facial-Digital 1 regulates the neuronal differentiation of embryonic stem cells. *Stem Cells and Development*. May;20(5):831-41
6. Babrauskas, V., Lucas, D., Eisenberg, D., **Singla, V.**, Dedeo, M., Blum, A. (2012). Flame retardants in building insulation: a case for re-evaluating building codes. *Building Research & Information*, 40(6), 738–755. doi:10.1080/09613218.2012.74453
7. Brownell, S. E., Hekmat-Scafe, D.S., **Singla, V.**, Seawell, P.C., Conklin-Imam, J.F., Eddy, S.L., Stearns, T., Cyert, M.S. (2015) A high-enrollment course-based undergraduate research experience improves student conceptions of scientific thinking and ability to interpret data. *CBE Life Sciences Education*, 14(2), 14-ar21. doi: 10.1187/cbe.14-05-0092
8. Hekmat-Scafe, D.S., Brownell, S.E., Seawell, P.C., Malladi, S., Conklin-Imam, J.F., **Singla, V.**, Bradon, N., Cyert, M.S., Stearns, T. (2016) Using yeast to determine the functional consequences of mutations in the human p53 tumor suppressor gene: An introductory course-based undergraduate research experience in molecular and cell biology. *Biochemistry and Molecular Biology Education*. doi: 10.1002/bmb.21024
9. Mitro, S.D., Dodson, R.E., **Singla, V.**, Adamkiewicz, G., Elmi, A.F., Tilly, M.K., Zota, A.R. (2016) Consumer product chemicals in indoor dust: A quantitative meta-analysis of U.S. studies. *Environmental Science & Technology*. doi: 10.1021/acs.est.6b02023

10. Zota, A.R., **Singla, V.**, Adamkiewicz, G., Mitro, S.D., and Dodson, R.E. (2017) Reducing chemical exposures at home: opportunities for action. *Journal of Epidemiology and Community Health*. (In press)

CONFERENCE ABSTRACTS

1. Poster presentation (2009) Evolution Symposium, **California Academy of Sciences**, San Francisco, CA. *Awarded prize for outstanding poster presentation*
2. Poster presentation. (2008) **American Society for Cell Biology Meeting**, San Francisco, CA.
3. Poster presentation (2005) **EMBL Workshop on Centrosomes and Spindle Pole Bodies**, Heidelberg, Germany.
4. Poster presentation (2005) **Society for Developmental Biology Meeting**, San Francisco, CA.

AMERICAN PUBLIC HEALTH ASSOCIATION
For science. For action. For health.

August 10, 2018

The Honorable Andrew Wheeler
Acting Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Re: Comments on Problem Formulation Documents for Risk Evaluations Conducted under the Toxic Substances Control Act as Amended;[1] Comments on "Application of Systematic Review in TSCA Risk Evaluations" Guidance Document[2]

Dear Acting Administrator Wheeler:

On behalf of the American Public Health Association, a diverse community of public health professionals that champions the health of all people and communities, I appreciate the opportunity to comment on: (1) problem formulation documents for risk evaluations that the U.S. Environmental Protection Agency is conducting under the Toxic Substances Control Act as amended and (2) EPA's "Application of Systematic Review in TSCA Risk Evaluations" guidance document.

TSCA is EPA's primary source of authority for evaluating and managing the health and environmental risks presented by approximately 85,000 industrial chemicals.[3] Unfortunately, the problem formulation documents indicate that the agency intends to conduct risk evaluations that are incomplete and likely to underestimate risk. Specifically, the agency plans to *ignore* numerous exposures to these chemicals. By considering only some exposures and not others, EPA likely will conclude that the total level of exposure to a chemical is lower than it truly is.

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[1] APHA has submitted these comments to the dockets for nine chemicals: 1-bromopropane (EPA-HQ-OPPT-2016-0741); carbon tetrachloride (EPA-HQ-OPPT-2016-0733); 1,4-dioxane (EPA-HQ-OPPT-2016-0723); cyclic aliphatic bromide cluster (HBCD) (EPA-HQ-OPPT-2016-0735); methylene chloride (EPA-HQ-OPPT-2016-0742); N-methylpyrrolidone (EPA-HQ-OPPT-2016-0743); perchloroethylene (EPA-HQ-OPPT-2016-0732); pigment violet 29 (EPA-HQ-OPPT-2016-0725); and trichloroethylene (EPA-HQ-OPPT-2016-0737). APHA has submitted separate comments to the docket for asbestos (EPA-HQ-OPPT-2016-0736).

[2] APHA also has submitted these comments to the docket for the "Application of Systematic Review in TSCA Risk Evaluations" guidance document (EPA-HQ-OPPT-2018-0210).

[3] EPA, *About the TSCA Chemical Substance Inventory* (last updated Sept. 14, 2016), https://www.epa.gov/tsca-inventory/about-tsca-chemical-substance-inventory.

The agency then may determine incorrectly that this lower level of exposure does not present an unreasonable risk of injury to health or the environment, even when the true level of exposure does present such a risk. The decision to ignore chemical exposures is unlawful and lacks scientific credibility. EPA should include all exposures to these chemicals in its risk evaluations.

In addition, the Systematic Review Guidance describes how the agency intends to identify, evaluate, and integrate scientific information for TSCA risk evaluations. The guidance will be pivotal to the conduct and ultimately the scientific credibility of these evaluations. Yet the guidance is inconsistent with the best available science and has not been peer reviewed by independent experts. The current draft diverges from established techniques in use in the scientific community. I urge the agency to comply with its own Peer Review Handbook, to arrange for peer review of the guidance by the National Academy of Science, and to revise the guidance based on the results of this peer review prior to relying upon it to conduct systematic reviews for TSCA risk evaluations.

EPA's Exclusions of Exposures from the Risk Evaluations Are Unlawful and Lack Scientific Credibility

EPA's problem formulation documents indicate several ways in which the agency intends to ignore exposures to the chemicals. First, TSCA requires EPA to "conduct risk evaluations…to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment…*under the conditions of use*." TSCA § 6(b)(4)(A) (emphasis added). In general, "the conditions of use" of a chemical include the manufacture, distribution in commerce, processing, use, and disposal of the chemical. EPA has decided to ignore conditions of use and resulting exposures, either by declaring that certain activities are not conditions of use or by acknowledging that the activities are conditions of use but nonetheless declaring that they will not be included in the risk evaluation. These actions by the agency lack both legal and factual support.

Second, EPA has decided to exclude entire exposure pathways, such as inhalation of a chemical in ambient air or ingestion of a chemical in drinking water, from the risk evaluations. These exclusions rely on a flawed analysis of TSCA and other environmental statutes. Furthermore, EPA admits the exclusions will disregard important risks of injury to health.

Exclusions of Conditions of Use

The exclusion of certain activities from the risk evaluations is unlawful. As noted above, TSCA requires EPA to evaluate the risks presented by "a chemical substance" under "the conditions of use." The language of the statute clearly directs the agency to evaluate the risk presented by a chemical substance in total and does not provide for picking and choosing among conditions of use when conducting a risk evaluation. Even if EPA did possess the authority to include only some conditions of use and not others, however, the agency still has failed to support its exclusions with information provided in the problem formulation documents.

In many cases, it appears that EPA has obtained information via unverified communications with companies that once engaged and still may be engaged in activities that constitute conditions of use. These include manufacturers, processors, distributors, commercial users, and companies involved in disposal of one or more of the chemicals. It does not appear that EPA has taken

meaningful steps to verify information provided by companies or their representatives. This is inappropriate due to the obvious conflicts of interest with respect to risk evaluations for chemicals that once were or still are important to their businesses. For example, EPA has concluded that "domestic manufacture of HBCD has ceased" based primarily on assurances provided by two recent manufacturers of the flame retardant.[4] The agency does not indicate how it verified these assurances or how it will ensure that the purported cessation will continue in the future.

EPA relies on information from entities even after concluding that the information is not credible. For example, the agency relies on information from "several racing authorities" to conclude that dioxane is no longer used as a fuel additive in car racing.[5] Even though the racing authorities "could not provide credible information on…whether [dioxane] is currently used at all," the agency nonetheless determined that "fuels and fuel additives" are not a condition of use for the purposes of the 1,4-dioxane risk evaluation and will be excluded.[6]

Even if the information provided by a company is accurate, the company remains free to resume any activity at any point in the future absent a regulation stating otherwise. Such an activity therefore remains a "reasonably foreseeable" condition of use under the statute. Furthermore, accurate information that may be provided by one company or subset of companies cannot be assumed to represent the activities of all current or future firms within an industry. Yet EPA makes this assumption. The agency has excluded domestic manufacture of expanded polystyrene (EPS) resin and extruded polystyrene (XPS) masterbatch from the HBCD evaluation based on reports by "all *major* North American manufacturers…of EPS resin" and comments by "*major* producers" of XPS masterbatch (emphasis added), respectively.[7] These reports cover only manufacturers or producers that the agency considers "major." They cannot represent the activities of any other manufacturers of EPS resin or XPS masterbatch, including any future manufacturers.

At a minimum, if EPA is told that manufacture, import, and processing of a chemical has ceased, the agency should demand legally binding certification of such cessation from *every* previous manufacturer, importer, and processor of the chemical. Furthermore, the agency should promulgate a significant new use rule under TSCA § 5(a) so that, if and when manufacture, import, or processing of the chemical does occur in the future, the activity must be reported to EPA.

Exclusions of Exposure Pathways

In addition to ignoring conditions of use, EPA intends to disregard entire pathways of exposure to chemicals. By disregarding these pathways, EPA will narrow the scopes of the risk

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[4] EPA, *Problem Formulation for Cyclic Aliphatic Bromides Cluster (HBCD)* 20 (May 2018), https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/cyclic-aliphatic-bromides-cluster-hbcd-cluster-problem (hereafter, "Problem Formulation for HBCD").

[5] EPA, *Problem Formulation of the Risk Evaluation for 1,4-Dioxane* 18 (May 2018), https://www.epa.gov/sites/production/files/2018-06/documents/14-dioxane_problem_formulation_5-31-18.pdf (hereafter, "Problem Formulation for 1,4-Dioxane").

[6] *Id.*

[7] Problem Formulation for HBCD at 21.

evaluations further. For example, even if domestic manufacture of 1,4-dioxane is included in the scope of the risk evaluation, inhalation of 1,4-dioxane in ambient air or ingestion of 1,4-dioxane in drinking water as a result of releases by domestic manufacturers will be excluded. In addition, for every chemical except pigment violet 29, EPA argues it can ignore exposures resulting from disposal.[8] By excluding pathways, the agency will ignore potential exposure to more than 68 million pounds of industrial chemicals released each year.[9] EPA's rationale for excluding pathways disregards TSCA and, by the agency's own admission, ignores unreasonable risks of injury to health.

According to the agency, exposure pathways will be excluded when they fall under "other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist[.]"[10] There are key differences between the requirements imposed by "other environmental statutes" and the requirements imposed by TSCA. For example, EPA intends to exclude inhalation of methylene chloride in ambient air.[11] The agency claims that, because methylene chloride is listed as a hazardous air pollutant under the Clean Air Act, this pathway is "adequately assess[ed] and effectively manage[d]" under another statute and need not be considered under TSCA.[12] This is incorrect. EPA manages hazardous air pollutants by requiring source categories to reduce emissions based on what is achievable using certain technologies. The agency does not require source categories to eliminate all emissions, and the remaining emissions can present significant risks. In the case of methylene chloride in ambient air, there is no reason to believe that exposure and risk are effectively managed. As the agency acknowledges, "levels of methylene chloride in the ambient air are widespread and shown to be increasing."[13] EPA is required to evaluate the risk presented by chemicals under TSCA. This includes any risks to vulnerable populations. The agency cannot escape this requirement by ducking behind unrelated statutes that impose separate requirements to protect public health.

EPA admits that excluding exposure pathways will neglect unreasonable risks of injury to health presented by the chemicals. For example, the agency said it intends to exclude exposure to 1,4-dioxane in drinking water because drinking water contaminants may be regulated under the Safe Drinking Water Act.[14] (Notably, the agency does not regulate 1,4-dioxane under the Safe Drinking Water Act, nor has it proposed to do so.) EPA acknowledges that "[t]he general population may ingest 1,4-dioxane via contaminated drinking water."[15] EPA reports that 341

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[8] *See, e.g.,* EPA, *Problem Formulation of the Risk Evaluation for Carbon Tetrachloride (Methane, Tetrachloro-)* 50-51 (May 2018), https://www.epa.gov/sites/production/files/2018-06/documents/ccl4_problem_formulation_05-31-18.pdf.

[9] Environmental Defense Fund, *Pruitt EPA Illegally and Dramatically Undermines Authority to Limit Dangerous Chemicals under Reformed Chemical Safety Law* (Jun. 1, 2018), http://blogs.edf.org/health/2018/06/01/pruitt-epa-illegally-and-dramatically-undermines-authority-to-limit-dangerous-chemicals-under-reformed-chemical-safety-law.

[10] EPA, *Problem Formulation of the Risk Evaluation for Methylene Chloride (Dichloromethane, DCM)* 46 (May 2018), https://www.epa.gov/sites/production/files/2018-06/documents/mecl_problem_formulation_05-31-18.pdf.

[11] *Id.* at 54.

[12] *Id.*

[13] *Id.* at 39.

[14] Problem Formulation for 1,4-Dioxane at 31.

[15] *Id.* at 43.

water systems have measured 1,4-dioxane at concentrations associated with an excess cancer risk greater than or equal to one in one million.[16] This level of risk "has often been considered a "benchmark" above which EPA has concerns for exposure to the general population" — that is, the agency has considered this level of risk to be unreasonable.[17] Because EPA is excluding drinking water exposure to 1,4-dioxane from the risk evaluation, however, this unreasonable risk will be ignored.

EPA's Use of the Systematic Review Guidance Would Violate TSCA Science Standards

EPA's Systematic Review Guidance describes how EPA intends to identify, evaluate and integrate scientific information used in TSCA risk evaluations. The guidance will shape, for example, whether and to what extent the agency considers a study finding that exposure to a chemical was associated with a particular adverse health effect. TSCA requires EPA to "use scientific information, technical procedures, measures, methods, protocols, methodologies, or models, employed in a manner *consistent with the best available science*" and to "consider as applicable…the extent of independent verification or *peer review* of the information or of the procedures, measures, methods, protocols, methodologies, or models." § 26(h) (emphasis added). Yet the guidance is not consistent with the best available science nor has it been peer reviewed by independent experts. EPA's reliance on this version of the guidance would violate TSCA.

The guidance is not consistent with best practices for systematic review. The guidance includes hundreds of pages of data quality criteria that EPA will use to assign numeric scores to individual studies.[18] The agency says it may disregard a study based on the numeric score assigned to it.[19] This is an outdated approach. NAS discourages the use of numeric scoring in systematic review, noting that "[i]n recent years, systematic review teams have moved away from scoring systems to assess the quality of individual studies," in part because scoring systems have not been validated and different systems can produce radically different results.[20] Notably, systematic reviews conducted by EPA's Integrated Risk Information System do not utilize numeric scoring,[21] and neither should systematic reviews conducted under TSCA.

Surprisingly, EPA has not subjected the guidance to peer review. This is a major omission. In addition to ignoring TSCA's requirement to consider the extent of peer review of the scientific information and technical procedures used by the agency, relying on the guidance when it has not been peer reviewed would harm the scientific credibility of the TSCA program. As EPA's

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[16] *Id.* at 31.
[17] EPA, *New Chemicals Decision-Making Framework: Working Approach to Making Determinations under Section 5 of TSCA* 4 (November 2017), https://www.epa.gov/sites/production/files/2017-11/documents/new_chemicals_decision_framework_7_november_2017.pdf.
[18] EPA, *Application of Systematic Review in TSCA Risk Evaluations* 30 (May 2018), https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf.
[19] *Id.* at 33.
[20] Institute of Medicine, *Finding What Works in Health Care: Standards for Systematic Reviews* 132 (2011), https://www.nap.edu/catalog/13059/finding-what-works-in-health-care-standards-for-systematic-reviews (hereafter, "NAS Systematic Review Report").
[21] NAS, *Progress Toward Transforming the Integrated Risk Information System (IRIS) Program* 43-52 (2018), https://www.nap.edu/catalog/25086/progress-toward-transforming-the-integrated-risk-information-system-iris-program.

own Peer Review Handbook states, "Peer review enhances the credibility and acceptance of the decision based on the work product," which in this case is the decision to regulate or not regulate a chemical under TSCA based on a risk evaluation and determination.[22] EPA should seek peer review of the guidance by NAS, which has published several reports on the conduct of systematic review for chemical exposure and its application by federal agencies.[23]

EPA Must Evaluate Risks to Workers and Other Vulnerable Subpopulations and Ensure Adequate Protections

TSCA requires EPA to determine whether a chemical presents an unreasonable risk of injury to the general population and/or to "potentially exposed or susceptible subpopulations." § 6(b)(4)(A). A potentially exposed or susceptible subpopulation is any "group of individuals within the general population…who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population…such as infants, children, pregnant women, workers, or the elderly." § 3(12). It is well understood, for example, that pregnant women, children, and infants are uniquely susceptible to chemical exposures.[24] TSCA imposes a duty on EPA to ensure that vulnerable subpopulations are protected from chemical risks, and it is imperative that the agency conduct risk evaluations, make risk determinations, and promulgate risk management regulations in accordance with this duty.

In particular, TSCA provides new tools to protect workers from occupational exposures to a wide variety of chemicals encountered while on the job. Workers face significant risk of harm from chemical exposures but they are not adequately protected by regulations of the Occupational Safety and Health Administration. OSHA has adopted comprehensive health standards on just a few dozen chemicals since the agency was established in 1971, and most of these standards were issued before 1990.[25] Furthermore, tens of millions of workers are not covered by the Occupational Safety and Health Act. EPA's duty to protect workers and other vulnerable subpopulations under TSCA fills in gaps in the law that have allowed workers to go unprotected from chemical hazards.

Conclusion

TSCA now provides an opportunity to evaluate and manage the health and environmental risks presented by tens of thousands of industrial chemicals that to date have received scant attention from EPA. Seizing this opportunity will require the agency to conduct risk evaluations that

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[22] EPA Science and Technology Council, *Peer Review Handbook* 21 (2015), https://www.epa.gov/sites/production/files/2016-03/documents/epa_peer_review_handbook_4th_edition.pdf.

[23] *See, e.g.,* NAS, *Progress Toward Transforming the Integrated Risk Information System (IRIS) Program* 43-52 (2018), https://www.nap.edu/catalog/25086/progress-toward-transforming-the-integrated-risk-information-system-iris-program; NAS Systematic Review Report.

[24] Project TENDR: Targeting Environmental Neuro-Developmental Risks, *The TENDR Consensus Statement*, 124 Environmental Health Perspectives A118 (2016), https://ehp.niehs.nih.gov/ehp358; Patricia D. Koman, et al., *Examining joint effects of air pollution exposure and social determinants of health in defining "at-risk" populations under the Clean Air Act: susceptibility of pregnant women to hypertensive disorders of pregnancy*, 10 World Medical and Health Policy 1 (2018).

[25] U.S. Government Accountability Office, *Workplace Safety and Health: Multiple Challenges Lengthen OSHA's Standard Setting* (April 2012), https://www.gao.gov/assets/590/589825.pdf.

include all exposures, to use the best available science, and to ensure adequate protections for vulnerable subpopulation. We therefore respectfully request that EPA reexamine its problem formulation documents and Systematic Review Guidance prior to completing the draft risk evaluations for the chemicals it currently is evaluating.

Thank you for taking our comments into consideration. Please feel free to contact me with any questions regarding our views on EPA's proposals.

Sincerely,

Georges C. Benjamin, MD
Executive Director

Problem Formulation Documents - Public Comments

FULL LIST OF COMMENTS

#	Submitter	Attachments (#)	Category (RegNex, Editorial, Exposure, Fate, Engineering, Human Health, Eco Health, PESS, Policy, Other, Systematic Review, General)	Document Section #	Comment	Applies to ALL (Y/N)	Check all docs where comment was found or applies: 1-BP	1,4-Dioxane	PERC	PV29	HBCD	CCl4	DCM	NMP	TCE	Asbestos	RAD POC	Docket #	Action Needed
1	ACC	3	General	N/A	Section 26 of TSCA mandates that EPA make science-based decisions under Sections 4, 5, and 6 of TSCA in a manner consistent with the best available science and the weight of the scientific evidence. EPA's development of a structured process to identify, evaluate, and integrate evidence from both the hazard and exposure assessments developed during the TSCA risk evaluations is appropriate and will provide increased transparency into the TSCA risk evaluation process.	Y	N	N	N	N	N	N	N	N	N	N			
2	ACC	3	General	N/A	In general, EPA should make the results of its systematic review process available as part of the docket for each risk evaluation, including its selection of key studies and study quality evaluations.	Y	N	N	N	N	N	N	N	N	N	N			
3	ACC	3	General	N/A	EPA has identified those conditions of use that will be within the scope of the risk evaluations, as well as those that will be excluded. The risk evaluation rule makes clear that EPA should focus on those conditions of use that raise the greatest potential for risk. ACC generally supports the approach taken to addressing conditions of use within each of the 10 problem formulations. This approach allows EPA to be efficient, while still addressing the highest priority conditions of use that pose the greatest potential risk.	Y	N	N	N	N	N	N	N	N	N	N			
4	ACC	3	General	N/A	The problem formulation documents present a thoughtful approach to identifying current uses that are appropriate for inclusion within the scope of the risk evaluation. We also appreciate EPA's efforts to explain why the conditions of use that are not within scope will be excluded. ACC encourages continued stakeholder engagement with manufacturers and users of these chemicals throughout the risk evaluation process to ensure the best available information is used.	Y	N	N	N	N	N	N	N	N	N	N			
5	ACC	3	General	N/A	As EPA gains more experience conducting TSCA risk evaluations for high priority chemicals, it would be useful if the Agency would develop a framework that articulates its process for deciding when conditions of use are in or out of scope. This would help EPA streamline future efforts, provide greater public understanding of EPA's decisions, increase transparency and reproducibility, and enable industry to identify the types of information that may be most helpful for manufacturers, processors, and downstream users to develop and/or share with EPA. Developing a framework would also help industry anticipate which conditions of use will be the likely focus in future assessments so that they can direct resources efficiently to develop and/or gather information relevant to EPA's potential risk evaluations and facilitate proactive data collection efforts.	Y	N	N	N	N	N	N	N	N	N	N			
6	ACC	3	General	N/A	"Section 9(d) of TSCA imposes a general requirement on EPA to consult and coordinate with other federal agencies for purposes of "achieving the maximum enforcement" of TSCA while imposing the "least burdens of duplicative requirements on those [subject to TSCA]." This Section 9(d) coordination requirement has existed since TSCA was originally enacted and was unchanged by the 2016 amendments. Section 9(d) is a general policy directive that applies to EPA for all TSCA implementation activities. The risk evaluation rule also contains a general consultation provision that codifies the statutory requirement for interagency collaboration during the risk evaluation process." The principle driving this coordination requirement is that EPA should avoid imposing unnecessary or duplicative burdens on regulated entities and avoid regulatory actions best taken by another agency or under other EPA authority. This necessarily includes all manner of Agency interaction with regulated entities, including submission of information, docket management, responses to comments, and other engagement with multiple regulatory bodies. Where non-TSCA regulatory schemes are sufficiently effective at addressing risk, EPA may properly exclude covered conditions of use from the scope of the risk evaluation.	Y	N	N	N	N	N	N	N	N	N	N			
7	ACC	3	Exposure	N/A	Regarding occupational exposures, EPA should consult early with OSHA in the risk evaluation process—certainly at the earliest stages of the risk evaluation and well before the scope is released. This consultation should continue throughout the risk evaluation. None of the 10 problem formulations make clear what consultation may have occurred, or when it occurred. Although the problem formulations do identify available occupational exposure levels (OELs), i.e., PELs, TLVs, and IDLH values, additional information should be provided regarding the factors EPA will take into consideration when evaluating OELs. For example, consideration should be given to whether the OEL includes current toxicological and epidemiological data to support the development of the threshold limit value. EPA also presents summarized personal monitoring air samples obtained from OSHA inspections, but it is not clear how these data were obtained from OSHA and under what circumstances the data were gathered.	Y	N	N	N	N	N	N	N	N	N	N			
8	ACC	3	Exposure	N/A	EPA should give preference to direct data obtained for uses being evaluated with consideration given to how the data were gathered (i.e., workplace exposure monitoring data are gathered on a more routine basis while OSHA monitoring is conducted typically in compliance with the OSHA Technical Manual for 8 hours and the sample will generally involve the scenario or tasks in which the highest exposure is expected).	Y	N	N	N	N	N	N	N	N	N	N			
9	ACC	3	General	N/A	For purposes of 9(d) compliance, it would be helpful if subsequent risk evaluation scopes offer more detail regarding EPA's coordination with other agencies, including information such as consultation plans, data shared, etc. We encourage EPA to include such a coordination plan in future scopes and to include these plans in the draft risk evaluations, including notations where consultation has occurred.	Y	N	N	N	N	N	N	N	N	N	N			
10	ACC	3	Exposure	N/A	It would be helpful for EPA to describe the decision criteria/framework by which it will evaluate whether to include occupational exposures in the scope of a risk evaluation. This description was not included in the 10 problem formulation documents.	Y	N	N	N	N	N	N	N	N	N	N			
11	ACC	3	General	N/A	EPA should apply a tiered approach throughout the risk evaluation process–from screening/prioritizing chemicals to conducting risk evaluations–under amended TSCA. This is essential to enable EPA to meet TSCA's statutory deadlines for completing risk evaluations, adhere to TSCA's robust scientific standards, and enable both EPA and the regulated community to apply limited resources efficiently.	Y	N	N	N	N	N	N	N	N	N	N			

12	ACC	3	General	N/A	When a screening-level assessment is insufficient to conclude a lack of risk to exposed populations, EPA should take steps to refine the risk evaluation allowing more accurate quantification of potential risks. The scoping/problem formulation documents indicate where the EPA feels it has sufficient information and where additional information and use of higher-tier tools is warranted. In situations where EPA may need to perform higher-tier assessments for the risk evaluation, more information is needed on the types of data and techniques that EPA will utilize. For example, EPA should indicate how probabilistic risk assessment (PRA), uncertainty analyses, and the use of statistical tools such as Bayesian statistics would be used at a higher tier within the overall problem formulation framework. A tiered, iterative approach is critical to the production of high quality risk evaluations based on the best available information.	Y	N	N	N	N	N	N	N	N	N	N			
13	ACC	3	Exposure	N/A	The value of tiered exposure assessment is well-established. In its 1992 guidelines on exposure assessment,10 EPA discusses the value of tiered exposure assessments from screening-level assessments to more complex assessments. This perspective was reiterated in EPA's 2016 peer review draft update of the 1992 guidelines. The 2016 draft update included specific discussion of considerations in tiered assessments, as well as the notion of "fit for purpose" assessments, stating "[t]he type and purpose of an exposure assessment determine the data and information requirements." The EPA Office of Research and Development (ORD) ExpoBox tool box for exposure assessors identifies exposure assessments tools by tier and type, both screening-level and refined, for planning, scoping, and problem formulation. The purpose of tiered exposure approaches is well understood: to identify uses of chemicals that, under very conservative (e.g., maximum) exposure assessment assumptions, are not likely to pose a health risk. Depending on the conditions of use, the exposure assessment information can be used either to identify a chemical as a low priority or to be factored into the overall risk evaluation. Exposures that initially exceed hazard benchmarks in Tier-1 exposure assessments would require more refined, higher-tiered approaches to exposure assessments. This would include the application of more realistic parameters related to the likely duration, intensity, frequency, and number of exposures and more realistic exposure scenarios to more accurately quantify actual risks of the chemical. The importance of EPA using a tiered approach to exposure assessment in its TSCA risk evaluations cannot be overstated. A tiered approach allows for both a more rapid, yet systematic, approach for assessing conditions of use in a first-tier screen, so that resources are used effectively when a refined exposure assessment is necessary for those conditions of use that do not "pass" a first-tier screen. well-defined, tiered exposure approach can lead to greater efficiencies in chemical risk evaluations under TSCA. Congress clearly valued such efficiency highly as evidenced by the aggressive deadlines it set for EPA to conduct TSCA risk evaluations. Congress also directed the Agency to consider the likely duration, intensity, frequency, and number of exposures under the conditions of use.	Y	N	N	N	N	N	N	N	N	N	N			
14	ACC	3	Exposure	N/A	The value of tiered exposure approaches in risk evaluations is even broader than exposure assessment. This was discussed in the Health and Environmental Sciences Institute's (HESI) Coordinated Risk Assessment in the 21st Century (Risk21) project. A review article published in 2014 discussing Risk21's principles and framework for decision-making in human health risk assessment emphasizes that problem formulation for risk assessment should not be a hazard-driven process, but instead should start with exposure, focusing on exposure scenarios of greatest concern integrated with hazard information to support risk-based decision making. The article suggests this approach would result in an early estimate of potential human exposure in relevant populations, including susceptible populations, which would characterize the degree of specific toxicological data needs. The Risk21 framework also addresses two other principles: (1) additional data should be acquired "only if necessary and when they add value" and (2) flexibility, "such that a higher tier hazard assessment approach can be coupled with a lower tier exposure approach, and vice versa." Considerable progress has been made over the last several years in developing screening-level exposure prediction models for chemicals in commerce. These approaches can be of particular utility in conducting Tier-1 assessments for many chemicals. In the context of TSCA's risk evaluations, tiered-assessment concepts equip EPA with the tools it needs to meet TSCA's aggressive deadlines for completing risk evaluations of high priority chemicals. Tiered assessments also enable EPA to apply limited resources in an efficient manner. Using a clear, science-based tiered-assessment approach, EPA and the regulated community can perform exposure assessments in TSCA risk evaluations, enabling efficient decision-making.	Y	N	N	N	N	N	N	N	N	N	N			
15	ACC	3	Exposure	N/A	The draft problem formulation documents of the initial 10 chemicals mention the Agency's plans to use tiered exposure assessments in its risk evaluations of these chemicals, but the documents lack specifics. A clear "road map" showing EPA's approach to tiered exposure assessments is needed in EPA's scoping documents. Such a road map—or decision tree—would provide structure to EPA's approach to exposure assessments under TSCA. This structure would also be useful to explain how EPA will integrate the results of its tiered exposure assessments with the results from its tiered-hazard assessments in TSCA risk evaluations. A road map would signal to the regulated community the type of reasonably available exposure information EPA plans to rely upon, what additional exposure information might be needed, and what actions manufacturers could take early in the risk evaluation process to provide EPA the needed exposure information. EPA should delineate what kinds of data and information it could accept to refine lower-tier exposure assessments.	Y	N	N	N	N	N	N	N	N	N	N			
16	ACC	3	Exposure	N/A	Specifically, with respect to potential human exposures in the problem formulation documents, EPA should identify: -The screening-level exposure information/models EPA will use to address human exposure in Tier-1 exposure assessments; -The approach to hazard characterization and threshold EPA will use to ascertain the need for a higher-tier exposure assessment; -How EPA will communicate Tier-1 exposure screening-level results; -The higher-tiered information and models EPA will use to address human exposures, suggested by the results of the screening-level information/models; -How EPA might use tiered exposure evaluations for specific exposure scenarios (e.g., occupational, consumer, residential, etc.); -What kind of data and information EPA would accept (i.e. from stakeholders) to refine a Tier-1 screening exposure assessment.	Y	N	N	N	N	N	N	N	N	N	N			

17	ACC	3	Exposure	N/A	TSCA Section 26(l) requires EPA to develop "policies, procedures and guidance that the Administrator determines are necessary to carry out the amendments" of amended TSCA. EPA indicates its intent to use tiered approaches in TSCA risk evaluations, but guidance is needed. EPA should develop new, more specific guidance on its plans to use tiered approaches to exposure assessment in TSCA risk evaluations. In doing so, EPA must move beyond mere "concepts" and reference lists to specific information, models, and tools. As stated earlier, EPA should indicate how PRA, uncertainty analyses, and the use of statistical tools would be integrated as a higher tier assessment. Specific and transparent guidance is needed to understand how the Agency will conduct its exposure assessments so that manufacturers can provide the most relevant information early on in the process to the Agency and so that stakeholders understand the process. As stated earlier, EPA should indicate how PRA, uncertainty analyses, and the use of statistical tools would be integrated as a higher tier assessment. Such guidance will also allow stakeholders to provide additional information to refine initial lower tier exposure estimates. Further program-specific guidance is also needed for those manufacturers that plan to conduct risk evaluations for EPA's consideration and must conform to EPA's approach to risk evaluations should they do so. Guidance on tiered approaches will help streamline the risk evaluation process under TSCA and enable EPA to meet TSCA's new mandates.	Y	N	N	N	N	N	N	N	N	N	N	N			
18	ACC	3	Exposure	N/A	Canada's Chemical Management Plan (CMP), Australia's Inventory of Chemical Substances,23 and the EU's Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) program24 employ tiered approaches in their exposure assessment approaches for chemicals. EPA should review those approaches to ascertain their usefulness in new EPA guidance on tiered exposure assessments in TSCA risk evaluations.	Y	N	N	N	N	N	N	N	N	N	N	N			
19	ACC	3	Exposure	N/A	According to EPA's problem formulations, EPA plans to further analyze occupational exposures in nine of the 10 chemicals risk evaluations. EPA must be more transparent about its coordination with OSHA regarding its plans to address occupational exposure issues in TSCA Section 6 risk evaluations. The methods, models, and databases that the Agency uses to conduct its occupational exposure assessments must be adequate to satisfy TSCA's Section 26 standards for best available science and weight of the scientific evidence. EPA should be more transparent about the OSHA and NIOSH databases that EPA plans to rely upon in these risk evaluations. Greater transparency will provide manufacturers notice about the type of information EPA may not have, but may need, to conduct a realistic occupational exposure assessment.	Y	N	N	N	N	N	N	N	N	N	N	N			
20	ACC	3	Exposure	N/A	In eight of the problem formulation documents, EPA has identified OSHA's Chemical Exposure Health Data (CEHD) and NIOSH's Health Hazard Evaluation (HHE) program data as two major sources of occupational monitoring data that it will rely upon in the risk evaluations. However, EPA does not discuss what information in these databases it plans to rely upon; how representative the data are; what criteria EPA will use in deciding which data are or are not applicable for its exposure assessments; or how it plans to assess those data in the context of current OSHA regulations and industrial hygiene practices. EPA must provide greater detail about its use of the information in these OSHA and NIOSH databases to enable stakeholders to comment upon the data quality for the purposes for which EPA plans to rely upon the data, and to provide the Agency higher quality data where it exists.	Y	N	N	N	N	N	N	N	N	N	N	N			
21	ACC	3	Exposure	N/A	For instance, it is our understanding that the OSHA CEHD information does not include a description of the activities associated with the specific exposure measurements. Without this information, how will EPA be able to apply these results to the conditions of use identified for a chemical? Absent sufficient knowledge of activities associated with occupational exposure measurements, EPA might very well improperly assign exposure values to a certain condition of use/application. This could result in inappropriate conclusions about risk under specific conditions of use or risk management recommendations for protection of workers. It appears that this database reports non-detects (ND), but it does not specify the limit of detection (LOD). Without an understanding of the accuracy of the data, how will EPA use this data to inform estimates of exposure? In occupational settings, potentially hazardous exposures are eliminated or minimized by the use of training, industrial hygiene programs, engineering controls, closed systems, personal protective equipment (PPE), labeling, medical surveillance, etc. Over the past several decades, these engineering and industrial hygiene practices have continually improved. For example, as part of ACC's Responsible Care® Program, ACC member companies must implement ACC's Process Safety Code, which aims to supplement existing process safety requirements contained within the Responsible Care Management System® and RC14001® technical specifications. The Process Safety Code is intended to complement regulatory standards that, by necessity, focus on process safety at an individual facility. Another concern with the OSHA CEHD database is that much of the data were developed during inspections of facilities suspected of having high employee exposures. This suggests these data are not representative of occupational exposures from facilities that are in compliance with OSHA standards. EPA should address this fact in its quality review of the data/information underpinning its risk evaluations.	Y	N	N	N	N	N	N	N	N	N	N	N			
22	ACC	3	Exposure	N/A	ACC understands that some ACC members have provided EPA with occupational monitoring information for use by the Agency in problem formulations for some of the initial 10 chemicals, but this information was apparently not reflected in the problem formulations issued on June 11, 2018. EPA should be clear in the draft risk evaluations how such submitted occupational monitoring information was used to prepare the problem formulations and considered in the risk evaluation.	Y	N	N	N	N	N	N	N	N	N	N	N			
23	ACC	3	Exposure	N/A	EPA indicates it plans to further analyze occupational exposures in the draft risk evaluations in nine of the 10 problem formulations. EPA has conducted very few worker exposure assessments on existing TSCA chemicals in the past and its Exposure Factors Handbook does not address occupational exposures.EPA has occupational exposure tools that are designed for specific purposes. For example, ChemSTEER was developed as a conservative screening tool used to estimate workplace exposures and environmental releases for new chemicals that are manufactured and used in industrial/commercial settings. However, broad guidance is not currently available for evaluating occupational exposures under TSCA, in particular with respect to the evaluation of existing chemicals. EPA should develop new guidance for evaluating occupational exposures under TSCA. To develop this guidance, EPA should certainly consider its own information, models, and tools on occupational exposure. EPA should also update some of its older tools and methods to evaluate worker exposure. EPA should update its 1997 Generic Scenarios for industry-specific workplace release and exposure estimation to make certain they reflect current industry practice. Many industrial practices in use today go beyond the legal regulatory requirements of OSHA. EPA should consider current industrial hygiene practices as part of the conditions of use of manufacturing. Additional Generic Scenarios may need to be developed to cover conditions of use for which Generic Scenarios do not currently exist.	Y	N	N	N	N	N	N	N	N	N	N	N			
24	ACC	3	Exposure	N/A	It is also critical that EPA consider other information and tools available from OSHA, from the American Industrial Hygiene Association (AIHA), and from other jurisdictions to develop new occupational exposure guidance for TSCA purposes. EPA should consider the applicability of new models being used in Canada and the EU in their chemical regulatory programs. In considering information and tools from OSHA, AIHA, and other jurisdictions, EPA should also consider the adequacy and appropriateness of use of those tools in the TSCA context.	Y	N	N	N	N	N	N	N	N	N	N	N			

25	ACC	3	Exposure	N/A	With respect to dermal exposures, the problem formulation documents identify several models for application to four of the 10 chemicals. EPA's existing dermal exposure assessment guidance is primarily geared toward neat compounds in soil or water, and it is not clear whether this guidance is sufficient to evaluate chemicals encountered in industrial-use scenarios.	Y	N	N	N	N	N	N	N	N	N	N	N	N			
26	ACC	3	Exposure	N/A	For inhalation exposures, EPA has identified several models it plans to use in nine of the problem formulations. EPA guidance on potential inhalation exposures in occupational conditions of use under TSCA would be helpful.	Y	N	N	N	N	N	N	N	N	N	N	N			
27	ACC	3	Exposure	N/A	Guidance on occupational exposure assessment under TSCA should address how the Agency will consider standard industrial hygiene practices as well as how that information will be incorporated into its exposure assessments and how ultimately that information will be integrated into the risk evaluation. EPA should address and identify the specific information the Agency will need to accomplish these steps; the level of detail needed to enable the Agency to reach a determination about the adequacy of design measures such as: closed systems; the use of engineering controls and labeling requirements (e.g., the use of gloves or other PPE); and other operating procedures and management practices currently in use to eliminate or adequately minimize exposures in occupational settings. EPA should describe how these considerations are incorporated into a tiered occupational exposure assessment.	Y	N	N	N	N	N	N	N	N	N	N	N			
28	ACC	3	Exposure	N/A	EPA may need to gather information from industry regarding current occupational exposure protection practices. Industry may be able to facilitate access to that information. Manufacturers and organizations like AIHA may be able to help the Agency gather information about exposure data in occupational settings and industrial hygiene practices in various workplace situations. Ultimately, through such efforts, an EPA exposure factors handbook for occupational exposures could potentially be developed to address TSCA risk evaluation needs.	Y	N	N	N	N	N	N	N	N	N	N	N			
29	ACC	3	Exposure	N/A	Consistent with application of a tiered approach to assessing exposure, EPA should articulate what kind of data will be acceptable to refine an initial lower tier occupational exposure assessment. For example, if a screening level estimate from ChemSTEER needs to be refined, a road map (as described above) would be a key element of guidance to develop the necessary information to conduct a higher tier assessment.	Y	N	N	N	N	N	N	N	N	N	N	N			
30	ACC	3	Exposure	N/A	EPA should be more transparent about specific exposure models, margins of exposure and occupational exposure limits that it intends to utilize during the risk evaluation process. This will allow stakeholders to provide the Agency the exposure information it needs and can lead to better understanding as to how EPA will make risk determinations.	Y	N	N	N	N	N	N	N	N	N	N	N			
31	ACC	3	Exposure	N/A	ACC agrees with EPA's support for using tiered approaches generally, and in exposure modeling in particular. Under a tiered, iterative approach, screening-level tools, which are "protective by design," may be used initially. For substances that appear to present potential risks following a screening-level assessment, EPA should then proceed to use higher-tier tools. By beginning with screening-level assessments—which use more conservative assumptions and information than higher tier models—the Agency can optimize resource allocation by identifying exposure routes that present less risk early in the assessment process. When a Tier-1 screening assessment indicates low risk for a particular condition of use, the Agency should have a high degree of confidence that the potential risks are lower or perhaps nonexistent.	Y	N	N	N	N	N	N	N	N	N	N	N			
32	ACC	3	Exposure	N/A	It is critical that EPA establish clear and consistent guidance that defines when Tier-1 model results will trigger more detailed and refined subsequent assessments. In the problem formulation documents, EPA frequently cites regulatory and non-regulatory occupational exposure limits, but it neither clarifies how it would apply these limits during an exposure assessment, nor specifies a process that will be followed should the Tier-1 model results exceed these limits or margins of exposure. In the event that EPA uses threshold triggers for Tier-2 models within EPA's risk assessment process, the Agency must provide guidance regarding how it selects these values and provide stakeholders an opportunity to comment.	Y	N	N	N	N	N	N	N	N	N	N	N			
33	ACC	3	Exposure	N/A	Similarly, EPA should specify which exposure models—for all routes and populations—it intends to use during the risk evaluation process. In the problem formulations, EPA mentions several different models, but it does not provide rigorous guidance as to which tools will be used under which circumstances. Similarly, EPA does not identify specifically what it considers to be "higher tier models." Exposure models vary in terms of the purposes for which they are used, their input requirements, and assumptions. By providing a rationale for its model selection, the Agency will afford stakeholders an opportunity to provide appropriate data and contribute relevant information to EPA during its risk evaluations.	Y	N	N	N	N	N	N	N	N	N	N	N			
34	ACC	3	Exposure	N/A	EPA also should be clear about the use of modeled vs. measured data in evaluating exposure. For example, if measured data are rejected in favor of modeled estimates, the rationale for such a decision needs to be clear.	Y	N	N	N	N	N	N	N	N	N	N	N			
35	ACC	3	Exposure	N/A	EPA participates in the OECD's Working Party on Exposure Assessment (WPEA). In that capacity, EPA has been a global leader helping harmonize chemical use categories and developing standard exposure/emission scenario documents (ESDs) for occupational exposure assessments for chemical regulations. ACC expects that EPA will use these standard exposure scenarios in its occupational exposure assessments, but that is not clear from the problem formulation documents. EPA should clarify this point in its draft risk evaluations of these 10 chemicals and in any new guidance the Agency develops on exposure assessments under TSCA.	Y	N	N	N	N	N	N	N	N	N	N	N			
36	ACC	3	Exposure	N/A	In addition, EPA should develop additional standard exposure scenarios for both worker and consumer exposures under TSCA. Standard exposure scenarios would assure greater consistency in EPA exposure assessments; improve exposure model parameters; and help industry understand what specific information EPA needs in exposure assessments for TSCA risk evaluations. In short, standard exposure scenarios would improve efficiencies when conducting TSCA risk evaluations, which are critical given TSCA's statutory deadlines. EPA may want to consider stakeholder workshops to discuss ways in which standard exposure scenarios might be developed in the US. If so, EPA should also ensure that standard scenarios developed under REACH be discussed and considered at such workshops since many of these may be useful in TSCA as well.	Y	N	N	N	N	N	N	N	N	N	N	N			
37	ACC	3	Exposure	N/A	EPA Should Explain What Additional Ecological Exposure Assessment Tools Are Available. The screening-level approaches described in the problem formulation documents are appropriate for this step (i.e., E-FAST), but EPA should identify acceptable tools/methods for higher-tier refinement when necessary. Screening-level exposure analysis may be suitable in cases where estimates do not exceed the Concentration of Concern (COC). EPA should explain how it would use higher-tier information, if provided.	Y	N	N	N	N	N	N	N	N	N	N	N			
38	ACC	3	Exposure	N/A	EPA has indicated that environmental exposure data may be available for some of these 10 chemicals in the EPA Discharge Monitoring Report tool, EPA's STOrage and RETreival (STORET) system, USGS National Water Quality Assessment (NAWQA) program, and other sources. Some of these data sources may not be current and therefore may not represent the best available information. EPA should clarify exactly how it would use such data to establish a national, regional, or local environmental exposure estimate.	Y	N	N	N	N	N	N	N	N	N	N	N			
39	ACC	3	Exposure	N/A	EPA should also clarify how it will quantify and assess (or exclude) naturally-occurring sources of chemicals for assessment during exposure estimation.	Y	N	N	N	N	N	N	N	N	N	N	N			

40	ACC	3	Exposure	N/A	EPA's Consumer Exposure Model (CEM) is mentioned as the preferred tool for estimating consumer exposures in several of the first 10 chemicals' risk evaluations. This model is publicly available. However, another model mentioned by EPA is the Multi-Chamber Concentration and Exposure Model (MCCEM). This model is available on EPA's exposure tools website, but in a version (Windows 95 operating environment) that will not run on currently available platforms. EPA should ensure that all the models it uses in its assessments are publicly available in a form that is accessible to the general public, complete with explanations on how to use the model and how the exposure endpoints are estimated.	Y	N	N	N	N	N	N	N	N	N	N	N			
41	ACC	3	Exposure	N/A	The problem formulations for most of the 10 chemicals indicate that the chemical is found in either formulated products used by consumers or in articles with which consumers could come into contact. It is not clear how EPA will assess consumer exposures to these products. The exposure assessments must be able to estimate the consumer exposures from these chemicals based on whether they are found in formulated products or articles.	Y	N	N	N	N	N	N	N	N	N	N	N			
42	ACC	3	Exposure	N/A	For chemicals that are primarily in articles, the approach and rationale for estimating consumer exposures should be described in detail because exposure assessments from articles are a new area of assessment. Industry and other stakeholders may not be familiar with the rationale and approaches used to estimate exposures from articles. The scientific basis for determining exposures from chemicals in articles must be established for the Agency to meet the statutory standard that requires TSCA risk assessments to quantify the likely (i.e., having a high probability of being true) duration, intensity, frequency, and number of exposures under the conditions of use. EPA should clearly identify the criteria for and scope of the tools chosen to be used in each circumstance.	Y	N	N	N	N	N	N	N	N	N	N	N			
43	ACC	3	Exposure	N/A	For exposure assessments, EPA may need to make decisions about which products to focus on in the assessments among the various potential products in which the chemical may be found. To conduct the consumer exposure assessment, the assessor may need to focus on representative products in some of these use categories. The product types chosen to be used in the exposure models, the exposure routes, most relevant exposure scenarios, exposure endpoints, and rationale for the choices must be described. The greater the clarity and transparency of these explanations, the greater the likelihood the final assessment will be understood.	Y	N	N	N	N	N	N	N	N	N	N	N			
44	ACC	3	Exposure	N/A	EPA states in several of the problem formulations that TRI data will be used as a source of information on releases to the environment. TRI data may have a role to play as an element in chemical prioritization, but these data also have limitations. EPA states on the TRI website: [The Toxics Release Inventory (TRI) provides data about environmental releases of toxic chemicals from industrial facilities throughout the United States, measured in pounds. The quantity of releases, however, does not indicate the level of health risk posed by the chemicals. Although TRI data can't tell you whether or to what extent you've been exposed to these chemicals, they can be used as a starting point in evaluating potential risks to human health and the environment.] EPA readily acknowledges in its TRI National Analysis 2016: Releases of Chemicals that "[h]uman health risk resulting from exposure to toxic chemicals are determined by many factors…" These factors include environmental fate, individual exposures, chemical properties, and concentration, none of which are furnished through the TRI. For a chemical to present a risk, there must be a sufficient pathway and exposure, factors that TRI does not address. EPA should acknowledge and explain the limited value of TRI data in risk evaluation.	y	N	N	N	N	N	N	N	N	N	N	N			
45	ACC	3	Exposure	N/A	Biomonitoring information is identified in several of the problem formulations as a type of data/information source for TSCA risk evaluations, but there is limited discussion of how or where it would be used. EPA should address in guidance the specific biomonitoring information it would rely upon in TSCA risk evaluations and how it would be used. Canada uses "biomonitoring equivalents" in its risk assessments under the Canadian Management Plan (CMP). EPA should examine how those values, as well as Canada's assessments that are based upon them, might be used in the TSCA exposure assessments.	y	N	N	N	N	N	N	N	N	N	N	N			
46	ACC	3	Human Health	N/A	It is important that a multidisciplinary review process, which integrates hazard information and data from in vitro and in vivo studies across different biological levels of organization for a given exposure scenario, be established for hazard evaluation, data review, and decision making contexts. Typically, this should be a transparent and structured analysis using the Bradford Hill causal considerations and, in particular, biological plausibility and empirical support (dose response, temporal concordance and consistency). The hazard information must be relevant to the specific exposure scenario and the integration of data should be applied initially for each data stream (epidemiology, in vivo, mechanistic) across similar types of study endpoints. The lines of evidence (human epidemiology, in vivo toxicity and mechanistic) must then be integrated using a transparent and objective approach. Through such an integrated assessment, evaluators use the entire body of studies and the full weight of the scientific evidence. This approach avoids the pitfalls of selecting the lowest statistically significant finding of a response in a given study (as a default) without adequately framing the risk hypotheses and integrating data from different sources. EPA states in the general response to comments on the initial 10 scope documents that it anticipates using data from alternative test methods for the risk evaluations. This is consistent with the mandate under TSCA Section 4(h) to "reduce and replace, to the extent practicable, scientifically justified, and consistent with the policies of this title, the use of vertebrate animals in the testing of chemical substances or mixtures…"	Y	N	N	N	N	N	N	N	N	N	N	N			
47	ACC	3	Human Health	N/A	ACC supports EPA's continued efforts to identify, develop, and integrate new approach methodologies (NAMs) for regulatory decision-making according to the EPA OPPT Strategic Plan to Promote the Development and Implementation of Alternative Test Methods. It is important that sufficient scientific confidence in each NAM be established for its intended application before use as a key piece of evidence in a hazard evaluation and limitations be acknowledged. It is equally important that exposure information, at a fit-for-purpose level of resolution, is available to place these data into a risk context.	Y	N	N	N	N	N	N	N	N	N	N	N			
48	ACC	3	Human Health	N/A	EPA acknowledges that it must further analyze the MOA for cancer risk in the problem formulations. ACC supports that analysis. The AOP framework is a tool to systematically organize available data and knowledge that describes scientifically plausible and causal relationships across multiple levels of biological organization between a molecular initiating event (MIE) and subsequent key events (KEs), culminating in an adverse outcome (AO) potentially relevant to risk assessment. EPA researchers have been instrumental in developing AOPs and tools to facilitate the further development, review, and use of AOPs in scientific and regulatory endeavors. Tools such as the AOP wiki can be mined for additional data and organizational principles as well as domains of applicability for various identified MOAs associated with chemicals. Thus, whether evidence generally aligns or does not align with any proposed or known MOAs and/or AOPs should be a necessary consideration in integrating evidence to reach conclusions.	Y	N	N	N	N	N	N	N	N	N	N	N			

49	ACC	3	Human Health	N/A	The Agency's focus on dose-response data and models reflects the fact that toxicology has evolved over the past 35 years from a largely observational field of study to a discipline that applies advanced scientific techniques and knowledge to investigate how chemicals interact with biological systems at the molecular, cellular, organ, and organism levels to understand the biological basis for the induction of toxicity. As a consequence of rapid advances in scientific understanding and the application of this knowledge to regulatory science policy and risk assessments, risk assessors can now evaluate biological events leading to toxicity and consider how, in a dose-response manner, these events relate to potential risks to human health. Despite the significant progress, movement away from default assumptions has been slow to occur, particularly in certain EPA programs. Failure to recognize and act on advances in scientific knowledge and the best available, most relevant scientific data and dose response models wastes significant research and development investments. It is also contrary to the TSCA Section 26 requirement that EPA rely upon best available science in science-based Section 6 decisions.	Y	N	N	N	N	N	N	N	N	N	N	N			
50	ACC	3	Human Health	N/A	In its 2005 Cancer Guidelines, EPA is clear that when risk assessments are performed using only one set of procedures, it may be difficult for risk managers to determine how much health protection is built into a particular hazard determination or risk characterization. EPA's Cancer Guidelines state:[When there are alternative procedures having significant biological support, the Agency encourages assessments to be performed using these alternative procedures, if feasible, in order to shed light on the uncertainties in the assessment, recognizing that the Agencymay decide to give greater weight to one set of procedures than another in a specific assessment or management decision.] In addition, the Agency says: [If critical analysis of agent-specific information is consistent with one or more biologically based models as well as with the default option, the alternative models and the default option are both carried through the assessment and characterized for the risk manager. In this case, the default model not only fits the data, but also serves as a benchmark for comparison with other analyses. This case also highlights the importance of extensive experimentation to support a conclusion about mode of action, including addressing the issue of whether alternative modes of action are also plausible.] These statements are related to comment 50.	Y	N	N	N	N	N	N	N	N	N	N	N			
51	ACC	3	Human Health	N/A	EPA's Office of Pesticide Programs (OPP) has adopted the World Health Organization (WHO)/International Programme on Chemical Safety (IPCS) MOA framework for organizing, evaluating, and integrating hazard and dose response information. The same approach should be adopted for TSCA assessments. The MOA framework can be used to illustrate the key events in a known toxicity pathway to address whether a reported statistically-significant response is consistent with what is expected based upon knowledge of the biological responses comprising the pathway. It should be noted that even if early biological responses/perturbations are detected, these observations are not necessarily adverse or precursors to adverse effects in living organisms because of adaptive or homeostatic mechanisms. To reliably predict toxicity, key events need to be causally linked to adversity with a clear understanding of dose response/temporal key event relationships. EPA should adopt and use the standard MOA templates for both cancer and non-cancer endpoints, such as the dose/temporal concordance and species concordance templates. These templates have been incorporated by the European Chemicals Agency (ECHA) in implementing Europe's REACH program.	Y	N	N	N	N	N	N	N	N	N	N	N			
52	ACC	3	Human Health	N/A	Because the scientific justification for assessing human relevance and selecting dose-response extrapolation methods for quantifying risks at environmentally relevant levels of exposure is highly dependent upon the determination of the likely operative MOA, the Agency should implement a uniform, systematic and explicit approach for evaluating a chemical dataset, using hypothesized MOAs and the evolved Bradford Hill causal considerations, to integrate evidence and derive weight of the evidence (WOE) confidence scores for potentially relevant MOAs. This approach enables a side-by-side comparison of numerical WOE confidence scores for different hypothesized MOAs, including the default linear-no-threshold model, which permits better identification of the likely best MOA to use. The side-by-side quantitative MOA WOE confidence scoring method enhances transparency and improves communication amongst risk managers and the public. Furthermore, the best available science approach provides a transparent, scientifically sound justification for using the most likely operative MOA as the basis for selecting the most appropriate extrapolation method that corresponds to that MOA to then calculate potential risks to humans for environmentally relevant exposures.	Y	N	N	N	N	N	N	N	N	N	N	N			
53	ACC	3	Human Health	N/A	To illustrate this method, a case example has been developed based on data of rodent liver tumors induced by carbon tetrachloride (Attachment B-attached in the ACC coments on Problem Forumulation 46 August 2018). This case example used data and lines of evidence from previously published review articles, and relied on those authors' evaluations of the quality of the empirical evidence. Two hypothesized MOAs were evaluated: 1) induction of rodent liver tumors via a mutagenic MOA; and 2) induction of rodent liver tumors via a cytotoxicity MOA. The quantitative MOA WOE confidence scoring results of this case example indicate: (1) it is highly unlikely that carbon tetrachloride induces rodent liver tumors via a mutagenic MOA and (2) Cytotoxicity and sustained regenerative cellular proliferation is the like operative MOA for induction of liver timors in rodents by carbon tetrachloride; there are significant mechanistic data to support thos non-linear, non-mutagenic MOA. Based on the comparison of quantitative MOA WOE confidence scores, there is strong scientific support for using a threshold extrapolation approach for evaluating the cancer risks of carbon tetrachloride. (In contrast, scientific justification is lacking to support a linear, no threshold extrapolation method for evaluating its cancer risks.)	N	N	N	N	N	N	N	N	N	N	N	N			
54	ACC	3	Human Health	N/A	Finally, another challenge in extrapolating animal data to human data involves having an understanding of the relative toxicokinetics. Significant strides have been made using physiologically based pharmacokinetic (PBPK) data and models in risk assessment to improve the accuracy of deriving dosimetry considerations. However, it is important to recognize that some animal studies using conventional maximum tolerated doses (MTDs) are flawed and cannot be used to extrapolate to human doses because they exceed the kinetically-derived maximum dose (KMD). In a number of cases, substances show dose-dependent transitions in their mechanisms of toxicity. This circumstance needs to be evaluated appropriately.	Y	N	N	N	N	N	N	N	N	N	N	N			
55	ACC	3	Eco Health	N/A	EPA has used a simple approach to calculate the acute and chronic COCs, i.e., dividing the lowest study value by an assessment factor. Conservative, screening-level approaches, such as those utilized in the EPA's New Chemicals Program, can be appropriate to provide context at the problem formulation stage. However, in future scoping documents EPA should clarify the circumstances under which further, higher-tier evaluation would be triggered, if necessary (e.g. species sensitivity distribution, etc.).	Y	N	N	N	N	N	N	N	N	N	N	N			
56	ACC	3	Eco Health	N/A	EPA should identify more sophisticated higher-tier approaches it may use for determining a hazard threshold, especially for data rich chemicals. Toxicity information, and when available, knowledge of mechanisms, are integrated with exposure-response models for risk-based environmental safety decision making. Within an environmental context, the assessment of safety does not end at the organism, but includes extrapolation to populations, communities, and ecosystems. For ecological risk assessment, the possibility of obtaining site-specific population data is a critical option for higher-tier assessment.	Y	N	N	N	N	N	N	N	N	N	N	N			

57	ACC	3	Eco Health	N/A	EPA should also consider the unique physico-chemical properties that can impact substances' pharmacokinetics and toxicity profiles, as well as their environmental fate and distribution.	Y	N	N	N	N	N	N	N	N	N	N	N			
58	ACC	3	General	N/A	Conclusion: ACC commends EPA on its efforts to gather the best available information for the problem formulation documents for the initial 10 chemicals undergoing risk evaluation under amended TSCA. EPA has demonstrated some screening-level assessment techniques that allow EPA to focus on the conditions of use that pose the greatest potential for risk. However, in situations where EPA may need to perform higher tier assessments for the risk evaluation, more guidance and information is needed on the types of data and techniques that EPA will utilize. This will enable industry to better understand how to provide EPA with the information it needs to perform high quality risk evaluations.	Y	N	N	N	N	N	N	N	N	N	N	N			
59	APHA	1	Exposure	N/A	TSCA is EPA's primary source of authority for evaluating and managing the health and environmental risks presented by approximately 85,000 industrial chemicals. Unfortunately, the problem formulation documents indicate that the agency intends to conduct risk evaluations that are incomplete and likely to underestimate risk. Specifically, the agency plans to ignore numerous exposures to these chemicals. By considering only some exposures and not others, EPA likely will conclude that the total level of exposure to a chemical is lower than it truly is. The agency then may determine incorrectly that this lower level of exposure does not present an unreasonable risk of injury to health or the environment, even when the true level of exposure does present such a risk. The decision to ignore chemical exposures is unlawful and lacks scientific credibility. EPA should include all exposures to these chemicals in its risk evaluations.	Y	N	N	N	N	N	N	N	N	N	N	N			
60	APHA	1	Exposure	N/A	EPA's problem formulation documents indicate several ways in which the agency intends to ignore exposures to the chemicals. First, TSCA requires EPA to "conduct risk evaluations…to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment…under the conditions of use." TSCA § 6(b)(4)(A) (emphasis added). In general, "the conditions of use" of a chemical include the manufacture, distribution in commerce, processing, use, and disposal of the chemical. EPA has decided to ignore conditions of use and resulting exposures, either by declaring that certain activities are not conditions of use or by acknowledging that the activities are conditions of use but nonetheless declaring that they will not be included in the risk evaluation. These actions by the agency lack both legal and factual support.	Y	N	N	N	N	N	N	N	N	N	N	N			
61	APHA	1	Exposure	N/A	Second, EPA has decided to exclude entire exposure pathways, such as inhalation of a chemical in ambient air or ingestion of a chemical in drinking water, from the risk evaluations. These exclusions rely on a flawed analysis of TSCA and other environmental statutes. Furthermore, EPA admits the exclusions will disregard important risks of injury to health.	Y	N	N	N	N	N	N	N	N	N	N	N			
62	APHA	1	Exposure	N/A	The exclusion of certain activities from the risk evaluations is unlawful. As noted above, TSCA requires EPA to evaluate the risks presented by "a chemical substance" under "the conditions of use." The language of the statute clearly directs the agency to evaluate the risk presented by a chemical substance in total and does not provide for picking and choosing among conditions of use when conducting a risk evaluation. Even if EPA did possess the authority to include only some conditions of use and not others, however, the agency still has failed to support its exclusions with information provided in the problem formulation documents.	Y	N	N	N	N	N	N	N	N	N	N	N			
63	APHA	1	Exposure	N/A	In many cases, it appears that EPA has obtained information via unverified communications with companies that once engaged and still may be engaged in activities that constitute conditions of use. These include manufacturers, processors, distributors, commercial users, and companies involved in disposal of one or more of the chemicals. It does not appear that EPA has taken meaningful steps to verify information provided by companies or their representatives. This is inappropriate due to the obvious conflicts of interest with respect to risk evaluations for chemicals that once were or still are important to their businesses.	Y	N	N	N	N	N	N	N	N	N	N	N			
64	APHA	1	Exposure	N/A	For example, EPA has concluded that "domestic manufacture of HBCD has ceased" based primarily on assurances provided by two recent manufacturers of the flame retardant. The agency does not indicate how it verified these assurances or how it will ensure that the purported cessation will continue in the future.	N	N	N	N	N	Y	N	N	N	N	N	N			
65	APHA	1	Exposure	N/A	EPA relies on information from entities even after concluding that the information is not credible.	Y	N	N	N	N	N	N	N	N	N	N	N			
66	APHA	1	Exposure	N/A	For example, the agency relies on information from "several racing authorities" to conclude that dioxane is no longer used as a fuel additive in car racing. Even though the racing authorities "could not provide credible information on…whether [dioxane] is currently used at all," the agency nonetheless determined that "fuels and fuel additives" are not a condition of use for the purposes of the 1,4-dioxane risk evaluation and will be excluded.	N	N	Y	N	N	N	N	N	N	N	N	N			
67	APHA	1	Exposure	N/A	Even if the information provided by a company is accurate, the company remains free to resume any activity at any point in the future absent a regulation stating otherwise. Such an activity therefore remains a "reasonably foreseeable" condition of use under the statute. Furthermore, accurate information that may be provided by one company or subset of companies cannot be assumed to represent the activities of all current or future firms within an industry. Yet EPA makes this assumption.	Y	N	N	N	N	N	N	N	N	N	N	N			
68	APHA	1	Exposure	N/A	The agency has excluded domestic manufacture of expanded polystyrene (EPS) resin and extruded polystyrene (XPS) masterbatch from the HBCD evaluation based on reports by "all major North American manufacturers…of EPS resin" and comments by "major producers" of XPS masterbatch (emphasis added), respectively. These reports cover only manufacturers or producers that the agency considers "major." They cannot represent the activities of any other manufacturers of EPS resin or XPS masterbatch, including any future manufacturers.	N	N	N	N	N	Y	N	N	N	N	N	N			
69	APHA	1	Exposure	N/A	At a minimum, if EPA is told that manufacture, import, and processing of a chemical has ceased, the agency should demand legally binding certification of such cessation from every previous manufacturer, importer, and processor of the chemical. Furthermore, the agency should promulgate a significant new use rule under TSCA § 5(a) so that, if and when manufacture, import, or processing of the chemical does occur in the future, the activity must be reported to EPA.	Y	N	N	N	N	N	N	N	N	N	N	N			
70	APHA	1	Exposure	N/A	In addition to ignoring conditions of use, EPA intends to disregard entire pathways of exposure to chemicals. By disregarding these pathways, EPA will narrow the scopes of the risk evaluations further. In addition, for every chemical except pigment violet 29, EPA argues it can ignore exposures resulting from disposal. By excluding pathways, the agency will ignore potential exposure to more than 68 million pounds of industrial chemicals released each year. EPA's rationale for excluding pathways disregards TSCA and, by the agency's own admission, ignores unreasonable risks of injury to health.	Y	N	N	N	N	N	N	N	N	N	N	N			
71	APHA	1	Exposure	N/A	For example, even if domestic manufacture of 1,4-dioxane is included in the scope of the risk evaluation, inhalation of 1,4-dioxane in ambient air or ingestion of 1,4-dioxane in drinking water as a result of releases by domestic manufacturers will be excluded.	N	N	Y	N	N	N	N	N	N	N	N	N			

72	APHA	1	Exposure, RegNex	N/A	According to the agency, exposure pathways will be excluded when they fall under “other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist[.]” There are key differences between the requirements imposed by “other environmental statutes” and the requirements imposed by TSCA.	Y	N	N	N	N	N	N	N	N	N	N	N	N			
73	APHA	1	Exposure, RegNex	N/A	For example, EPA intends to exclude inhalation of methylene chloride in ambient air. The agency claims that, because methylene chloride is listed as a hazardous air pollutant under the Clean Air Act, this pathway is “adequately assess[ed] and effectively manage[d]” under another statute and need not be considered under TSCA. This is incorrect. EPA manages hazardous air pollutants by requiring source categories to reduce emissions based on what is achievable using certain technologies. The agency does not require source categories to eliminate all emissions, and the remaining emissions can present significant risks. In the case of methylene chloride in ambient air, there is no reason to believe that exposure and risk are effectively managed. As the agency acknowledges, “levels of methylene chloride in the ambient air are widespread and shown to be increasing.”	N	N	N	N	N	N	N	Y	N	N	N			
74	APHA	1	Exposure, RegNex	N/A	EPA is required to evaluate the risk presented by chemicals under TSCA. This includes any risks to vulnerable populations. The agency cannot escape this requirement by ducking behind unrelated statutes that impose separate requirements to protect public health.	Y	N	N	N	N	N	N	N	N	N	N			
75	APHA	1	Exposure	N/A	EPA admits that excluding exposure pathways will neglect unreasonable risks of injury to health presented by the chemicals.	Y	N	N	N	N	N	N	N	N	N	N			
76	APHA	1	Exposure	N/A	For example, the agency said it intends to exclude exposure to 1,4-dioxane in drinking water because drinking water contaminants may be regulated under the Safe Drinking Water Act. (Notably, the agency does not regulate 1,4-dioxane under the Safe Drinking Water Act, nor has it proposed to do so.) EPA acknowledges that “[t]he general population may ingest 1,4-dioxane via contaminated drinking water.” EPA reports that 341 water systems have measured 1,4-dioxane at concentrations associated with an excess cancer risk greater than or equal to one in one million. This level of risk “has often been considered a “benchmark” above which EPA has concerns for exposure to the general population” — that is,the agency has considered this level of risk to be unreasonable. Because EPA is excluding drinking water exposure to 1,4-dioxane from the risk evaluation, however, this unreasonable risk will be ignored.	N	N	Y	N	N	N	N	N	N	N			
77	APHA	1	PESS	N/A	TSCA requires EPA to determine whether a chemical presents an unreasonable risk of injury to the general population and/or to “potentially exposed or susceptible subpopulations.” §6(b)(4)(A). A potentially exposed or susceptible subpopulation is any “group of individualswithin the general population…who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population…such as infants, children, pregnant women, workers, or the elderly.” § 3(12). It is well understood, for example, that pregnant women, children, and infants are uniquely susceptible to chemical exposures. TSCA imposes a duty on EPA to ensure that vulnerable subpopulations are protected from chemical risks, and it is imperative that the agency conduct risk evaluations, make risk determinations, and promulgate risk management regulations in accordance with this duty. In particular, TSCA provides new tools to protect workers from occupational exposures to a wide variety of chemicals encountered while on the job. Workers face significant risk of harm from chemical exposures but they are not adequately protected by regulations of the Occupational Safety and Health Administration. OSHA has adopted comprehensive health standards on just a few dozen chemicals since the agency was established in 1971, and most of these standards were issued before 1990.25 Furthermore, tens of millions of workers are not covered by the Occupational Safety and Health Act. EPA’s duty to protect workers and other vulnerable subpopulations under TSCA fills in gaps in the law that have allowed workers to go unprotected from chemical hazards.	Y	N	N	N	N	N	N	N	N	N	N			
78	NTTC	1	PESS	N/A	Affirmed by the Supreme Court, it is the law of the land that federal agencies must fulfill a legally-binding trust responsibility to protect tribal trust resources and must uphold U.S.-Tribal treaty agreements. As the federal regulatory agency charged with environmental protection, this duty is relevant to EPA’s implementation of TSCA because tribes have high exposure to the natural environment, dietary reliance on local wild foods, and unique customary and traditional practices.Thus, under TSCA, tribes meet the definition of an exposed subpopulation, and EPA must adequately and transparently evaluate these exposures. The National Tribal Toxics Council (NTTC) is the Office of Pollution Prevention and Toxics (OPPT) Tribal Partnership Group to represent the collective interests of the 576 federally-recognized sovereign tribal nations across the United States, located within all 10 EPA regions. Together, 6.1 million tribal members are represented.	Y	N	N	N	N	N	N	N	N	N	N			
79	NTTC	1	PESS	N/A	A risk assessment based on the HBCD Problem Formulation will not be protective of tribal, rural, or urban subsistence populations as it fails to identify exposed subpopulations. Consequently, unless the Problem Formulation is changed to explicitly address these populations, the EPA Administrator will fail to carry out requirements as mandated by Congress in TSCA, as amended, June 22, 2016.	N	N	N	N	N	Y	N	N	N	N	N			
80	NTTC	1	PESS	N/A	NTTC takes issue with the methodology used in identifying relevant literature for the scoping document. Arguably, the greatest change in TSCA is the mandate of health-based assessment and the inclusion of sensitive and exposed subpopulations in identifying the health risk of chemicals to the American people. Yet, while tribal based risk scenarios are readily available, they are not addressed in the Problem Formulation, and there is no evidence that an attempt was made to include them. Tribes are simply not mentioned, whether it be in the literature search or bibliography, the narrative, or conceptual model. The same holds for ethnic-urban subsistence and rural subpopulations.	N	N	N	N	N	Y	N	N	N	N	N			

81	NTTC	1	PESS, Exposure	N/A	The EPA Office of Solid Waste is aware that permitted unlined municipal, and construction and demolition landfills are prevalent in Indian Country. The practice of open burning in burn barrels is widespread, and in Alaska Native villages the entire community wastestream is regularly burned without emissions control under a RCRA permit. Wild foods that the tribes depend on for their diet can be contaminated with HBCD via leachate and smoke, and whole communities can be exposed via inhalation and direct contact with wastes. Extruded and Expanded Polystyrene (XPS and EPS) insulation products are ubiquitous in Alaska and are used in ceilings, floors, interior walls, outside finished exterior walls, foundations and foundation wings, road beds, and more. The construction and demolition waste products, both residential and commercial, are brought to the unlined municipal landfills and dumpsites, or to unlined project-specific dumps. Nearly three-quarters of villages are within one mile of these disposal sites and their diets are dependent on locally hunted, fished, and gathered foods. Over eighty percent of these villages practice open burning, and because the sites are proximate, smoke from these disposal practices is commonly smelled by village residents. Even under the EPA's narrow Conditions of Use requirement, the resultant exposure scenarios for Alaska tribes, as well as Alaska rural residents that comprise more than half the population of the state, are left out. Many tribes are small communities with members being exposed in multiple ways. For example, the same worker who helped in the sawing of EPS board may be the landfill worker that carries the board to the dump and burns it, then goes home to their family where, now part of the community's "bystander" population, they have additional exposures by breathing the smoke, and consuming food and water that is contaminated from leachate.	N	N	N	N	N	Y	N	N	N	N	N			
82	NTTC	1	Exposure, General	N/A	Beyond the clear primary issue to Tribes of the absence of tribally-specific risk scenarios in the problem formulation, NTTC further takes issue with the following critical points that relate to the problem formulations in general and prevent the performance of a valid health assessment for tribes and other Americans as intended by Congress: -Omission of legacy use, particularly the use and disposal of products that are still in active service life. For example, it is unclear why the widespread use and disposal of millions of computers and other electronics known to contain HBCD is not considered in the problem formulation. -Omission of conditions of use considered to be under the purview of other Federal Environmental Statutes that focus primarily on priority pollutants. TSCA was amended specifically because Congress found that these same existing environmental laws did not adequately protect the American people. -Omission of products knowingly or reasonably foreseen to incorporate HBCD and the complete omission of recycled products due to a perceived 'lack of intention' in fitting the Administrator's narrowly defined Conditions of Use. For example, the use and disposal of picture frames, food trays, coolers, and other products knowingly made with recycled EPS of high HBCD content is not considered. The decisions taken by EPA on these points were spurious and each are clearly inconsistent with the science and purpose of risk assessment and TSCA itself.	Y	N	N	N	N	N	N	N	N	N	N			
83	NTTC	1	PESS	N/A	The following relevant language is excerpted from the Toxic Substances Control Act of 2016, as amended, pertaining to potentially exposed or susceptible subpopulation and to high-priority substances, and from the U.S. EPA Office of Chemical Safety and Pollution Prevention's May 2018 Problem Formulation for Cyclic Aliphatic Bromides Cluster (HBCD) respectively, with emphasis added relevant to the below comments. The term "potentially exposed or susceptible subpopulation" means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly. The Administrator shall designate as a high-priority substance a chemical substance that the Administrator concludes, without consideration of costs or other nonrisk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant by the Administrator. For HBCD, EPA considers workers, occupational non-users, consumers, and bystanders and certain other groups of individuals who may experience greater exposures than the general population due to proximity to conditions of use to be potentially exposed or susceptible subpopulations. EPA will evaluate whether groups of individuals within the general population may be exposed via pathways that are distinct from the general population due to unique characteristics (e.g., life stage, behaviors, activities, duration) that increase exposure, and whether groups of individuals have heightened susceptibility, and should therefore be considered potentially exposed or susceptible subpopulations for purposes of the risk evaluation.	N	N	N	N	N	Y	N	N	N	N	N			
84	NTTC	1	PESS, General, Exposure	N/A	As currently practiced, the proposed conceptual models of the first ten problem formulations issued May 2018 do not meet the standard of relevance and representation for Tribal peoples, and therefore the model implementation process is essentially moot, and the applicability of the model to the 6.1 million people that Tribes represent is irrelevant.	Y	N	N	N	N	N	N	N	N	N	N			
85	NTTC	1	General, Exposure	N/A	We use the commonly accepted definitions of key terminology in risk assessment science. The following excerpts are drawn from the International Programme on Chemical Safety (IPCS) glossary (2004)3 and the Principles of Characterizing and Applying Human Exposure Models (2005)4 as published by the World Health Organization. Exposure assessment is "The process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent, along with the number and characteristics of the population exposed. Ideally, it describes the sources, pathways, routes, and the uncertainties in the assessment" (IPCS, 2004). Exposure assessment is used in epidemiological studies to relate exposure concentrations to adverse health outcomes. Exposure assessment is also an integral component of risk assessment, the process that provides scientific information for risk management. Exposure assessment is based on exposure scenarios, which are defined as "A combination of facts, assumptions, and inferences that define a discrete situation where potential exposures may occur. These may include the source, the exposed population, the time frame of exposure, microenvironment(s), and activities. Scenarios are often created to aid exposure assessors in estimating exposure" (IPCS, 2004). An exposure model is a computational framework designed to reflect real-world human exposure scenarios and processes. A conceptual model is often illustrated by a block diagram, and it defines the physical, chemical and behavioural information and exposure algorithms by which the model mimics a realistic exposure scenario. ... The implementation of an exposure model should reflect the underlying conceptual model. Whenever the exposures of different subpopulations are expected to be different from each other, the exposure assessment probably needs to treat these subpopulations separately.	Y	N	N	N	N	N	N	N	N	N	N			

86	NTTC	1	General, Exposure	N/A	Model evaluation can be seen as a three-step process: -1.The conceptual model must be validated. ...The (causal) relationships between the model input events and the output events must be real, and the nature, or shape, of these relationships must be known — at least approximately. -2.The model implementation must follow the conceptual model. The definitions of input and output variables must effectively describe the events of the conceptual model, and the algorithms and equations must sufficiently follow the true (causal) relationships of these events. -3. Assessing the applicability of the model to a set of specific problems is possibly the most difficult step. This includes evaluating how well the input values really describe the target system. Usually the input values have been measured and contain random or systematic measurement errors. The measured input data range is a combination of data uncertainty and true inherent variability, and in some new applications it is essential to be able to differentiate between the two (e.g. when one or the other dominates the distribution). Sometimes other models, questionnaire data or expert opinions are used in place of measurements to assign values to input variables Each of these inputs may or may not accurately describe the characteristics of the target system. Thus, even when the model is conceptually valid and carefully implemented, the model outputs may not agree with the system outputs.	Y	N	N	N	N	N	N	N	N	N			
87	NTTC	1	General, Exposure, PESS	N/A	In several of the following sections, the NTTC provides wide-ranging explanation of the vast extent of activities within tribal lifeways, aspects of "the system" (as referenced above) that needs to be modeled in the risk assessment process. In section 7 NTTC provides a graphic image of tribal lifeways, to provide a visual sense of the realm of all natural resources within tribal lifeways, and multitude of exposure scenarios and exposure pathways by which tribal populations are put at greater risk because their tribal lifeways have not been contained with TSCA risk assessment and risk evaluation processes. Also, in section 7, NTTC proposes the draft Possible Tribal Exposures Conceptual Model which received preliminary review and informal comment in an NTTC meeting with EPA OPPT earlier this year. Though in draft form, NTTC emphasizes that by using this conceptual model when evaluating unreasonable risk of injury to health (or their environment) to a potentially exposed and susceptible subpopulations, EPA will thereby protect both tribal populations and other subpopulations.	Y	N	N	N	N	N	N	N	N	N			
88	NTTC	1	General, Exposure, PESS	N/A	In terms of subpopulations, consider how Barzyk (2010) discussed community-based risk assessment: "One of the primary differences between communities is in their patterns of exposure. ... Tools that isolate exposure routes and pathways for a given community and then incorporate toxicity information will lead to a better characterization of risk". This is key when considering potentially exposed and susceptible subpopulations, such as tribal groups whose patterns of exposure can be considered to be the "community" of an eco-region, e.g., the Pacific Northwest could encompass tribes and their lifeways from northern California, northerly along the Pacific coast into British Columbia, Canada and as far as the Prince William Sound in southcentral Alaska, U.S. -1. As currently practiced, the proposed conceptual models of the first ten problem formulations issued May 2018 do not meet the standard of relevance and representation for Tribal peoples, and therefore the model implementation process is essentially moot, and the applicability of the model to the 6.1 million people that Tribes represent is irrelevant. -2. Risk assessment of Tribal peoples for TSCA contaminants found in environmental media is relevant because Tribes are in contact with soil, sediment, and water as much or more than other population groups. -3. But the proposed problem formulations, and the risk assessments are not representative because they do not reflect nor model Tribal lifestyles. An entire population of people (6.1million strong) are not represented in any USEPA risk assessment work to date.	Y	N	N	N	N	N	N	N	N	N			
89	NTTC	1	General, Exposure, PESS	N/A	For millennia, tribal cultures were completely synonymous with and inseparable from the land and its resources. Tribes (used throughout this document) includes tribal people, resources, and other interests; interests (as sovereigns, seeking to govern/regulate tribal resources and as proprietors, i.e., holders of rights to land, water, fish, etc.) and the interests of individual Native people (whether they are tribal citizens or not; whether they live on a reservation or not); it is important to encompass tribal members who do not reside on tribal land, usual and accustomed areas, as well as treaty-protected resources; tribal lands as used in this report includes reservations, ceded lands, Usual and Accustomed areas (U&A) as well as communities inclusive of the Alaska Native Villages and Islanders and those without land bases. Continuing today, many tribes, tribal people and their clans are identified in their Native languages and in English translations as the name of singular or multiple seasonal locations or specific animals or insects, e.g. Water's Edge Clan (Navajo), People of the Herring Rock (Tlingit), Where the Water Cuts Through (Po-wo-ge-oweenge), Red Willow Place (Tua-Tah), People of the standing of projecting rock or stone (Seneca), The Place where the locusts were taken out (Cayuga), The River with the two logs across it (Chickaloon).	Y	N	N	N	N	N	N	N	N	N			
90	NTTC	1	Exposure, PESS	N/A	The Tribal Lifeway is the prime lifeway for those tribal members. Like a prime number cannot be formed by multiplying two smaller natural numbers, the prime Tribal Lifeway cannot be replaced by adapting other lifeways.	Y	N	N	N	N	N	N	N	N	N			
91	NTTC	1	Exposure, PESS	N/A	There are no viable or acceptable alternatives to subsistence resources, cultural-spiritual resources, and other resources of tribal lifeways. -Tribal people cannot buy meat, seafood or plant-based foods that are equivalent in calories and nutrients to their traditional and subsistence foods. Replacing resources based solely on calories or nutrition disregards the cultural and ceremonial aspects of the traditional resource. -- I.e., children and young adults learn to hunt, fish, gather, and then process the resources with an adult and/or elder. They learn the significance of the resource in relation to their ancestry and culture. They learn the inter-dependence of generations, or clans, or villages, or species. They learn the values and priorities of their culture. They learn traditional stories, the purpose of which includes cultural preservation, historical knowledge, and instilling moral values.	Y	N	N	N	N	N	N	N	N	N			

92	NTTC	1	Exposure, PESS	N/A	“Tribal lifeways” are inclusive of, but not limited to, economic, cultural, ceremonial, societal, political, recreational, and subsistence practices. Examples of tribal lifeways that may influence tribes’ exposure to chemicals in consumer products and the environment include but are not limited to: -Hunting, fishing, gathering, including accessing locations, processing collected items in the field and at home, -Constructing blinds in the field, drying racks, smoke houses -Husbandry (farming/growing) -Gathering, consumption, and everyday use of plants and plant materials (food, teas, medicines, salves, different types of combustibles for smoke generation, collection of firewood or tipi poles, etc.) -Water collection (untreated) -Collecting and processing materials for, and making baskets and other weaving, arts, tools, clothes (using feathers, skin, bones, hides, oils, antlers, etc.; wood, ivory and stone carvings) -Building/carving canoes, sweat lodges, fish weirs and traps, other structures -Bathing/sweat lodge use -Traditional medicine -Ceremonial or powwow activities (dancing, traditional games) -Smoke houses and ceremonies with smoke (fire, locally-harvested wood, sage, etc.) -Making and use of traditional pottery (made from local clays, dyes, etc.)	Y	N	N	N	N	N	N	N	N	N	N	N			
93	NTTC	1	General, PESS	N/A	Current Federal Indian Policy recognizes Tribal Sovereignty, Federal Trust Responsibility, and Government to Government Relationship, yet tribes today suffer health disparities, experience exposure pathways through tribal lifeways. Treaties are legally binding contracts between sovereign nations that establish those nations’ political and property relations. Article VI of the U.S. Constitution holds that treaties “are the supreme law of the land.” In return for taking vast Indian holdings and resources (i.e. land), the U.S. promised: Reservation Lands, Continued Sovereignty, Protection, Health Care, Education, Religious Freedom, Some Monies. Through the treaties they negotiated, tribes retained rights of self-government and jurisdiction. [excepn from the 1855 Treaty with Yakama] Tribal sovereignty means that tribes are independent nations with the right to govern themselves by: Forming their own government, adjudicate legal cases within its boundaries, levy taxes within their borders, establish its membership, and retain government-to-government relationship with the U.S.	Y	N	N	N	N	N	N	N	N	N	N	N			
94	NTTC	1	General, PESS	N/A	The Federal Government has a trust responsibility to protect tribal lands, assets, resources, and treaty rights, and uphold the promises made when treaties were made. With these recognized responsibilities and rights, Tribes have a unique legal status with the U.S. government. They are neither foreign nations, nor states. Tribes are distinct political communities defined in law as “domestic dependent nations.” In the 1831 Cherokee Nation v. Georgia decision, the Supreme Court described the obligation of the U.S. to tribes as that of a guardian to his wards. Subsequent decisions have made it clear that the agencies of the federal government are to be held to the most stringent “fiduciary” (trust) standards. “Trust lands” describe lands held in trust by the U.S. for the benefit of a tribe or individual tribal member which cannot be alienated or confiscated through eminent domain. Additional case law since that 1831 Supreme Court decision confirms federal trust responsibility and protection tribal culture, identity, and ways of life. "Moral obligation of the highest responsibility and trust"-Seminole Tribs v. U.S. (1942). The United States is the trustee of Indian reserved rights, including fishing rights. -See, e.g., Joint Board of Control v. United States, 862 F.2d 195 (1988), 198 (9th Cir. 1988); Muckleshoot Indian Tribe v. Hall, 698 F. Supp. 1504, 1510-1511 (W.D. Wash. 1988). The obligation of the United States as trustee of Indian resources and rights extends to all agencies and departments of the Executive Branch. -See Pyramid Lake Paiute Tribe v. Department of the Navy, 898 F.2d 1410, 1420 (9th Cir. 1990), Covelo Indian Community v. FERC, 895 F.2d 581, 586 (9th Cir. 1990). The right to resort to the fishing places in controversy was a part of larger rights possessed by the Indians, upon the existence of which there was not a shadow of impediment, and which were not much less necessary to the existence of the Indians than the atmosphere they breathed.”)U.S. v. Winans, 198 US 371 (1905). “…the Indians reiterated…that they wished to reserve the privilege of using the land for gathering, hunting, and fishing activities. They said that they could not live, deprived of these means of sustenance.Lac Court Oreilles Band of Chippewa Indians v. Leter P. Voigt, Seventh Circuit Court (1983).	Y	N	N	N	N	N	N	N	N	N	N	N			
95	NTTC	1	General, PESS	N/A	Tribal nations, their governments, and their enrolled tribal members and tribal descendants are present in the United States and continue their ancestral tribal lifeways. There are 573 federally recognized tribes: 229 in Alaska, 110 in California and 234 in 33 other states. There are 61 state recognized tribes in 12 states. As of 2017, the U.S. Census Bureau’s annual estimate of the Native American and Alaska Native population was 6.1 million which is 1.7% of the total U.S. population. Further, the Bureau projects that by 2050 the Native American and Alaska Native population will be 8.6 million, 2% of the total U.S. populations. The tribal nations with the largest populations include: Cherokee, Navajo, Choctaw, Chippewa, Sioux, Apache, Blackfeet, and Pueblo. The tribal lands—both trust lands and non-trust and non-reservation lands—accumulate to a collective geographical area today of 56 million acres which is equivalent to the size of Idaho state. Unfortunately, tribal people are afflicted by some of the least desirable statistics in the U.S.: the highest rates of suicide of any racial or ethnic group including white; highest rates of violence against women at more than double the rates of women of other races; overrepresentation in U.S. prisons and jails; historical and generational trauma from loss of people, lands and culture; posttraumatic stress disorder; more likely to have poorer overall physical and mental health and unmet medical and psychological needs; overrepresentation in the U.S. foster care system; and predisposition to heart disease, diabetes, and substance addiction. Many of these physical and mental health disparities are related to the historic and generational traumas, related to poverty induced by loss of people, lands, and language, related to the unmet obligations of the U.S. Government. These health disparities are exacerbated by environmental contaminants and pollutants in and around tribal resources. There is a legacy of toxic pollution on tribal lands and resources: "More than a century of hard rock mining has left a legacy of >160,000 abandoned mines in the Western USA that are home to the majority of Native American lands. ...Similar articles could be written focusing on impacts to tribal lands from coal strip mining, from the legacy of military bases, and from oil and gas development." Ineffective policies and the lack of infrastructure lead to environmental contamination through permitted exemptions to waste disposal allowing unlined landfills that accept household hazardous waste and unfiltered emissions from on-the-ground or other open burning. These exemptions also allow waste managers non-collection and non-treatment of landfill leachate. Additionally, tribal lands are commonly used for illegal waste dumping due to the significant void of law enforcement presence.	Y	N	N	N	N	N	N	N	N	N	N	N			

96	NTTC	1	General, PESS, Exposure	N/A	Despite attempts to disconnect tribes from traditional resources and tribal lifeways, tribal populations maintain a close relationship to the environment. The chemical exposures experienced by tribal people are not extremes of a general population range but consist of many discrete activities with legal protections. NTTC recognizes that prior to the Lautenberg Act, the burden of proof of toxicity was on the U.S.consumer. This is not adequate for the tribal community, especially considering the high-level consumption by tribal members of wild and natural resources as well as the U.S. government's trust responsibility and inability to provide safe water and sewer, and solid waste disposal on many Indian reservations and in many Alaska Native villages.	Y	N	N	N	N	N	N	N	N	N	N	N			
97	NTTC	1	PESS, Exposure	N/A	"Nonstandard exposure pathways occur under four circumstances: (1) qualitatively nonstandard exposures (e.g., dietary, medicinal, or cosmetic use of unusual plants), (2) quantitatively nonstandard exposure (i.e., high consumption rates, children eating dirt, a very large meal [e.g., feast of fish, whale, deer], high exposure relative to other foods, body size, or age), (3) both nonstandard and excessive exposure (i.e., applying a chemical or cosmetic to skin, potential exposure to chemicals through cultural activities such as sweat baths), and (4) inadvertent exposure as byproducts of other consumptive, social, or cultural practices (i.e., mercury exposure from cultural practices)."	Y	N	N	N	N	N	N	N	N	N	N	N			
98	NTTC	1	PESS, Exposure	N/A	Due to Tribal lifeways, as a whole, Tribal people ingest, inhale, contact, and dermally absorb chemicals from the natural environment more frequently, for longer periods of time, and in different ways, than the general population. Because Tribal lifeways are unique, these exposures are both qualitatively nonstandard (how people are exposed, such as basket grass softening via mouth) and quantitatively nonstandard (e.g. the amount of fish consumed). Tribal people spend longer periods of time and engage more often in the environmentl conducting unique outdoor traditional activites. Examples: Traditional water use (untreated water collection and consumption); hunting, fishing, gathering; ceremonies; social activities. Tribal people engage more often and spend more time interacting with environmental media, resources, and derived objects. Examples: Ceremonial objets (e.g., ceremonial feathers); artifacts (from generations past used for display, speical ceremonies, repatriation); art, tools from media (clay pots, reed baskets, baleen carving, etc.); food preparation and storage; steam baths with untreated water and full body immersion in untreated water.	Y	N	N	N	N	N	N	N	N	N	N	N			
99	NTTC	1	PESS, Exposure	N/A	Tribal people are substantially more likely to consume locally and regionally-obtained biota, whether plants, animals, or fish, and in greater quantities and greater diversity. Examples: plants; animals, large land mammals; fish, shell fish; large marine mammals. Regionally, certain traditional style of housing and practices, may present substantially greater exposures. E.g., adobe houses present durable dust and soil ingestion exposures off the charts. E.g., fish drying in Alaska with open burning of the community dump site several times per week, less than one quarter mile away, or fish, marine mammal, land animal dried and stored without a protective barrier in the arctic entryway where opened vehicle care products, paints, and other hazardous products are stored. Village housing, school, and landfill are all proximate within a compact area. Children playing in open space available like near vehicles, landfill sites, waste collection sites. There are a umber of facets related to traditional/cultural practices that are not reflected in the activity profiles currently used. Examples: Tribal people's lifestyles are largely seasonal and that dependence on season permeates their daily lives. Seasons are defined not by dates but by changes in the environment and the cycles of plants and animals tribes depend on. Work is often at home, and home environments reflect tribal lifestyles as do the handicraft or ceremonial objects they or extended family members may make. Dust is created by making handicraft and ceremonial objects, mixing with dust accumulated from dirt and gravel roads, furniture, and household products. Thus, dust inhalation and ingestion are major exposure pathways. Age groups are affected. Young children hunt and gather, elders may be more active in the environment longer than their peers in the general populations and serve as babysitters more often, usually living in the same home. Through established practices of sharing resources, the entirety of the Tribe can be exposed.	Y	N	N	N	N	N	N	N	N	N	N	N			
100	NTTC	1	General, PESS, Exposure	N/A	The below Graphic illustrates the unique exposures that Tribes face and that should be considered in any risk assessment procedure. The conceptual model that follows is intended for use in formulating the scope of any EPA chemical risk assessment. *See Conceptual Model Figures.* [Part 7, pages 10-11, presents a Conceptual Model of Tribal Exposures including a graphic reproduction and a flowchart]	Y	N	N	N	N	N	N	N	N	N	N	N			
101	NTTC	1	PESS, Exposure	N/A	Exposure measures or models aspects of frequency, duration, and intensity. As such there are multiple additional exposure routes that EPA must evaluate. NTTC maintains that resource use is another important factor to the risk paradigm which EPA is overlooking. EPA must consider whether tribes use different resources that results in different exposure routes(s) than the general consumer. For example, plants uptake the pollutants or pollutants adhere to plants, tribal members harvest those plant resources for customary and traditional foods and medicines, and for traditional arts such as basketry, thus demonstrating multiple exposure pathways including ingestion, dermal absorption on the hands, and in some cases, dermal absorption in the mouth from splitting roots or softening materials. The three steps in the process are (1) Identifying exposure pathways based on the media and resource that is contaminated, (2) Identifying the route of exposure (what is the portal of entry into the person), and (3) Developing exposure factors (the numerical representations of the exposures).	Y	N	N	N	N	N	N	N	N	N	N	N			
102	NTTC	1	PESS, Exposure	N/A	Thus, exposure assessors must consider data about three prime exposure factors, frequency, duration, and contact rate: -what products Tribes use in their daily lives (e.g., PBDE and/or HBCD-laden older upholstered furniture or bisphenol A (BPA)-infused plastics); -aspects of where they reside that may be non-standard, including but not limited to: proximity to an industrial emissions source, transportation corridor and utilidors, proximity to waste disposal burning and leachate, downriver of or adjacent to a contaminated site, closely-housed communities with only dirt roads, arctic entries where hazardous chemicals are co-located with food and water, aged home furnishings containing long-since banned chemicals breaking down into dust and thus increased inhalation and ingestion, rural locations more likely near open burning and more likely to have vehicles and other solid waste illegally disposed of in their environment, incomplete plumbing and incomplete kitchens—which are found in 7 percent of tribal homes compared with less than 2 percent of all U.S. households. For example, 36 percent of Alaska tribal area households have incomplete plumbing, incomplete kitchens, or overcrowding. -how much time tribes spend engaged in various activities at differing levels of cardiovascular vigor (e.g., sleeping, sitting, exercising, hunting) in various locations (e.g., indoors at work, outdoors in a garden, gathering wild foods in a national forest or a utility right-of-way sprayed with herbicides); -the quantities of various food, drink, and traditional medicinal items ingested; and -how all of these vary over a lifetime.	Y	N	N	N	N	N	N	N	N	N	N	N			

103	NTTC	1	PESS, Exposure	N/A	Examples of subsistence, traditional, and ceremonial-spiritual activities that should be considered affected by chemicals in consumer products and the environment include but are not limited to: -Collection and use of edible and medicinal resources and cultural materials on public lands such as utility rights of way, streambeds, and marshes. This may include wading and constant soaking of feet and hands in water during collection activities. -Preparation of traditional materials, including cleaning in surface water and other activities such as chewing reeds, sinew, and fish skins for additional uses. -High consumption of plants gathered and fish and animals (including shellfish and other invertebrates) collected locally, including non-standard consumption such as fish skin, fats and oils, or other parts of animals, most of which are not readily available in the supermarket. -Meditation, bathing, steam baths, cooking, cleaning, soaking traditional materials (also placed in mouth while conducting multiple activities), and drinking local surface and rain water and snow and ice melt. -Smoking fish/meats and hides, burning out canoes, cultural burning to stimulate material production, and heating rocks for cooking, shaping wood and sweat lodges. -Occupational and environmental exposures are also often overlooked. For example, a study of malignant mesothelioma found that Native American silversmiths routinely used asbestos mats to insulate worktables while making silver jewelry, which exposed them to a hazard, asbestos, that was seemingly unrelated to the occupational activity (silversmith).	Y	N	N	N	N	N	N	N	N	N	N	N			
104	NTTC	1	PESS, Exposure	N/A	Regarding the population scenario, the tribal population scenario is the most appropriate to use for risk assessments by EPA because TSCA requires EPA to protect the population of highest risk. Additionally, it is a federal trust responsibility to tribes under the U.S. government's moral and legal obligations to American Indians and Alaska Natives. EPA must use the fish consumption rates of subsistence fishers so that EPA accounts for aggregate exposure of those who rely heavily on locally sourced fish. Consider that EPA identified in the 2015 problem formulation for the HBCD cluster, the fish consumption rate of 142.5 grams based on subsistence fishers consumption rates (U.S. EPA, 2015a). Furthermore, there are EPA-accepted rates several times higher in Region 10.	Y	N	N	N	N	N	N	N	N	N	N	N			
105	NTTC	1	General, PESS, Exposure	N/A	NTTC supports EPA's comments on the September 30, 2015 technical call (U.S. EPA, 2015b) that EPA will evaluate additive exposures, such as oral exposures including fish consumption, drinking water consumption, potential for dust consumption and mouthing in the flame retardant risk assessments. However, in such an evaluation of oral exposures, EPA must include the high-end exposure approach with fish consumption rates of subsistence fishers.	Y	N	N	N	N	N	N	N	N	N	N			
106	NTTC	1	PESS, Exposure	N/A	Food other than fish: In the past EPA has stated it would not assess food other than fish because it is the purview of other agencies. EPA would do well to clarify that in this statement "food other than fish" refers to processed or manufactured food products and not the foods represented in tribal lifeways and other subsistence means. Otherwise, EPA is specifically excluding tribal citizens who consume large amounts of land and marine mammal tissue and fats in traditional foods including several species of ungulates, whale and seal, walrus, and sea lion. It also disregards other traditional foods of sea food, migratory birds and their eggs, and certain reptiles. EPA needs to consider these subsistence food sources for which numerous data sources are available from research conducted in the U.S. and other Arctic countries, such as Canada, Greenland and Norway. EPA is a member agency of the White House Cabinet; it is capable of collaborating with its sister agencies that would assess food other than fish, as well as gathering data from such agencies.	Y	N	N	N	N	N	N	N	N	N	N	N			
107	NTTC	1	PESS, Exposure	N/A	Source-based model is inappropriate for Tribal exposures. In working with OPPT and in preparing the document *Understanding Tribal Exposures to Toxics* , the NTTC requested that OPPT include tribal exposure in their chemicals risk assessments. In response, OPPT staff has requested NTTC to provide the necessary data to consider tribal scenarios. Although some tribes may have data that OPPT is requesting, it became evident that funding for tribal-specific research is needed to provide multiple scenarios for consideration. Chemical-specific monitoring is also needed to determine if TSCA Work Plan chemicals that OPPT is conducting risk assessment on are present in subsistence foods and those resources handled, utilized, or consumed in tribal lifeways. It is unlikely that tribes can generate the necessary analytical data or compile the information OPPT needs to consider exposure pathways for TSCA Work Plan chemicals without specific project funding or technical assistance by EPA to complete tribal risk assessments. Therefore, in addition to addressing OPPT-specific requests for tribal recommendations, NTTC expanded the scope of this report [NTTC 2015] to provide a foundation for requesting studies that could serve OPPT's needs for incorporating tribal-specific data and exposure scenarios into TSCA chemical risk assessments.	Y	N	N	N	N	N	N	N	N	N	N	N			
108	NTTC	1	PESS, Exposure	N/A	The LifeLine Group, Software Models, and Data Compendiums. The LifeLine Group, Inc. is a US 501(c)(3) non-profit organization that has developed peoplebased probabilistic modeling software that can account for non-standard diets and that has established peer-reviewed compendia of customized dietary files for the American Southwestand Mexican-Influenced diets, Alaska Traditional and Subsistence foods, and First Nations and Inuit in Arctic Canada traditional foods. To identify subpopulations (e.g., children, women, etc.) that are at greater risk, the LifeLine™ Community-Based Assessment Software can use a community's dietary and activity files created with the Dietary Record Generator© and Activity Record Generator© together with the contaminant residue data to present a community-specific exposure and risk assessment. The LifeLine Software can handle a full array of information and values, and describes how exposure and risk are distributed across a population as well as variability in exposure and risk due to day-to-day variation in contaminant or exposure levels. The LifeLine assessment can also examine health effects over the short and longer terms. The software is freely available and with appropriate expertise or assistance, can be used by communities as well as decision-makers at the local, state, provincial and national levels. For instance, for the Compendium of Alaska Traditional and Subsistence Dietary Files©, the LifeLine Group constructed the food consumption database for Alaska Native populations from a diverse array of information about dietary habits, food availability, and economics of the populations for whom there are no detailed food consumption surveys. This and the Dietary Files for the American Southwest™ provide high-quality data that is scientifically accurate, relevant, representative, and quantifiable for uniquely exposed and susceptible subpopulations while reducing the burden of needing chemical-specific data for every single exposure pathway, which is unlikely or nearly impossible for either tribes or EPA to collect. Further information on the relevance, data quality, and other principles to vet the data used in database construction is available at The LifeLine Group's website.	Y	N	N	N	N	N	N	N	N	N	N	N			
109	NTTC	1	PESS, Exposure	N/A	The durability of tribal environmental exposures may be orders of magnitude higher because Tribal peoples hunt and gather resources locally, then consume and use these local resources—not purchasing them at a grocery store where the meat, produce and other foods might come from any number of different sources and those locations vary over time. Further, for populations in urban areas, there are choices of various fish, meat, and produce in a grocery store, but not so from a subsistence area.	Y	N	N	N	N	N	N	N	N	N	N	N			

110	NTTC	1	General, PESS, Exposure	N/A	Mitigation by Avoidance or Replacement is Not an Option. When at least half of your diet is derived locally, you cannot stop eating that and switch to other foods. This type of mitigation action used in past risk management strategies, i.e., "don't consume more than X amount in Y timeframe," amounts to an unfunded mandate and forced cultural loss which is documented to lead to a range of societal ills that cause economic impact as well. As Ocampo wrote: Many First Nations [Indigenous People] peoples embrace a shared group identity whose substance is formed not just by one's relationship to the community but also to the land and one's ancestors, which may include plants, animals and other elements of nature. For example, traditional Native Hawai'ians consider the taro, a root staple that nurtures them, a physical ancestor now under their guardianship. Thus, reduction or dispossession of land/loss of stewardship of one's traditional plants and animals is experienced as an alienation or unmooring from the self, and in some communities is directly correlated with suicide (i.e., among the Guarani of Argentina - see Robinson, 2008).	Y	N	N	N	N	N	N	N	N	N	N			
111	NTTC	1	General, PESS	N/A	Whitbeck, Walls, Johnson, Morrisseau, & McDougall (2009) studied depression and historical loss among Indigenous adolescents, reporting that the measures of perceived historical loss and depression were separate but related constructs. Even when controlling for effecting influences such as family factors, discriminatory treatment, and proximal negative life events, an adolescent's perceived historical loss had independent effects on their depressive symptoms. The construct of historical loss is discussed in terms of Indigenous ethnic cleansing: military defeat, relocation to approximate penal colonies, starvation, neglect, forbidden to practice traditional means of survival and spiritual traditions, forced assimilation, children kidnapped and reeducated in settings that ignored kinship patterns, traditional language use punished, and efforts to replace traditional religious beliefs with Christianity, no specific end to government policies of assimilation, and no acknowledgement of ethnic cleansing or apology for it from the U.S. government. Reinschmidt, Attakai, Kahn, Whitewater, & Teufel-Shone (2016) developed the Stories of Resilience Model from interviewing and documenting Urban American Indian Elders' experiences of historical trauma and resilience. "For Indigenous people removed as children to boarding/residential schools or adopted by White families off reservation, this meant being removed from the tribal lands that were closely tied in with culture and traditions, including subsistence practices (farming and hunting), beliefs (traditional spirituality), and values (having respect for oneself and others). Separation from their families led to a loss of contact with relatives, especially elders, who passed on culture and traditions. Family members could no longer teach Native languages or engage children in family activities."	Y	N	N	N	N	N	N	N	N	N	N			
112	NTTC	1	General, PESS	N/A	Despite these historic and generational traumas, tribes have maintained cultural practices and values, and many tribes—but not all—maintained their Indigenous languages, stories, songs, and millennia of history. Thus, contrary to the efforts of colonization, assimilation, and attempts of genocide, research of Indigenous survivors is demonstrating that traditional spirituality, traditional practices, and cultural identity are proven protective factors for Indigenous children and adults. Further, there is accumulating evidence that traditional spirituality and practices are associated with alcohol cessation, are negatively related to depressive symptoms and suicidal behaviors among adults, and that they are associated with academic success, self-esteem, and prosocial behaviors among adolescents. Reinschmidt et al reference work by Kirmayer, Dandeneau, Marshall, Phillips, & Williamson (2011, 2012) supporting that community resilience is compatible with Indigenous values of relationships among people and with the environment. Distinct notions of personhood, where individuals are connected to the land and the environment, shape Indigenous ideas of individual resilience. "Land plays a critical sacrosanct role: it is itself sacred, with tribal-specific meaning, and it is also often directly connected to ritual sacred sites, where ceremonies and obligations are expected to be fulfilled." (Walters, Simoni & Evans-Campbell, 2002.)	Y	N	N	N	N	N	N	N	N	N	N			
113	NTTC	1	General, PESS	N/A	Resilience strategies in the context of the community included being "connected to the community," "involved in local community cultural activities," and "knowing one's Native language" were. Another elder's story demonstrated the connection between personal, family, and community resilience: "think the values that I picked up when I was growing up was making my baskets. That was one of the things that REALLY was good for me… I was taught by my mother and I learned that it really did help me. She …showed me how to prepare to make basket: first to go out and get the plants… I have to talk to the plants. You go up to the plants while you get them, so that it will help you, strengthen you, give you the courage to go on with your life and it's really not just making baskets. It's something that, it's sort of like a sacred secret. So that's what I did. I found out that that's REALLY helped me a lot. Not just making baskets, but keeping up with our tradition, something that our people used to make and use for many things. And also, I sell my baskets a lot so that helped me in many ways…that was my income when I couldn't work…" The Indigenous notion of personhood connects individuals to larger contexts, including family, community, spirituality and history. As described by the elders in the study, and in the literature (Kirmayer et al., 2009, 2012), the Indigenous notion of the self (or person or individual) is one of connectedness. Individual resilience thus must be understood as systemic in nature, because it refers to Indigenous notions of the individual that are characterized by connectedness. In telling their stories, elders talked about people who served as role models for them, about being role models themselves, and about the importance of role models. Most elders fondly remembered their grandparents, parents, or aunts. These relatives imparted knowledge and skills, including gardening, butchering, counseling others, being medicine men, and knowing traditions around birth and death.	Y	N	N	N	N	N	N	N	N	N	N			
114	NTTC	1	General, PESS	N/A	Healing among North American indigenous populations have common themes, shared health beliefs and a unified perspective of bio-psycho-socio-spiritual approaches and traditions, regardless of tribal-specific differences in healing practices, like feathers of different birds, sweat lodge or bonya steam bath, burning a dried herb or burning a fire dish of food. "The culture is the primary vehicle for delivering healing." Bassett, Tsosie, & Nannauck. 2012) "Native diets, ceremonies that greet the seasons and the harvests, and the use of native plants for healing purposes have been used to live to promote health by living in harmony with the earth." Koithan & Farrell (2010). Food from the land gives people life and brings them wellness. (Youth Taking Action, no date (n.d.)) "Alaska Natives have been nourished by foods from the land, air, and water for thousands of years (Alstrom & Johnson, n.d.)34. They have had a lifelong association with these foods, seeking them, harvesting them, cleaning them, preparing them to be eaten or stored, keeping the foods safe from loss of spoilage, and enjoying them as foods. People take great comfort from eating the foods they've grown up with. These foods can be very comfortable to eat in times of illness and healing, and are very rich in the nutrients necessary for good health. Native foods tend to be very good sources of nutrients like protein, iron, Vitamins A, D and E, and low in saturated fats and sugars. Native foods are the heart of culture and health. They provide close ties to the land and the seasons and the environment. Participating in harvesting, preparing, sharing and eating the foods along with others contributes to spiritual well being."	Y	N	N	N	N	N	N	N	N	N	N			

115	NTTC	1	PESS, Exposure	N/A	Disposal is a Condition of Use. Chemicals and/or their byproducts enter the natural environment via disposal of the consumer products. In the absence of considering disposal, EPA will not represent primary exposure pathways for Tribal populations, including the practice of traditional and customary activities, as well as for other populations. Disposal pathway regardless must be considered because contamination of media occurs even with best practice and facilities.	Y	N	N	N	N	N	N	N	N	N	N	N			
116	NTTC	1	PESS, Exposure	N/A	Activity profiles are not representational. It is known that chlorinated and brominated flame retardants (BFRs) are being released into our environment throughout the world (Bi et al., 2007;35 Kakimoto, Akutsu, Konishi & Tanaka, 200836; Tue et al, 2010;37 Vázquez & Rizo, 2014). Studies such as these include finding brominated flame retardants (BFRs) in multiple biological samples in exposed humans including in the breast milk of mothers living at e-waste recycling sites in China and Vietnam. As noted below, similar practices of openly burning solid waste occur under approved exemption to federal law in Alaska tribal villages, and occur in and near other tribal communities where law enforcement is minimal and underfunded.	Y	N	N	N	N	Y	N	N	N	N	N			
117	NTTC	1	PESS, Exposure	N/A	Not all disposal pathways are in lined landfills where hazardous material and construction and demolition (C&D) waste are disposed of in a separate landfill. There are 207 RCRA Subtitle D municipal waste unlined landfills in Alaska compared to nine lined landfills. The unlined landfills serve approximately half the population of the State and include most construction wastes. There are also occasionally site specific construction and demolition wastes that are universally unlined. Alaska rural landfills are unlined and allow open waste burning—two conditions that in 1976 were prohibited by federal statute for every other community in the United Sates because of the danger to community health, fire safety, and impact on the environment.	Y	N	N	N	N	N	N	N	N	N	N			
118	NTTC	1	PESS, Exposure	N/A	In fact, half of Superfund sites today are the unlined, open burned municipal landfills from the 1960's and 1970's. The lack of liner or emissions treatment means the sites are not designed to accept hazardous wastes. Much of this reason relates to distance from towns to their dump site and from the dump site to community drinking water sources. Wastes form leachate, which drains to drinking and subsistence water. About one third of Alaska offroad village dumpsites are within one quarter mile of a drinking water source, and about half flood each year. If wastes aren't discarded at the landfill, they are burned untreated and form toxic waste smoke and emissions, which is smelled in and around homes in about 80% of towns. About one fourth of these communities are breathing toxic emissions from their community's dumpsite at home, in town, every day for hours. While not many health studies have been carried out specific to villages, in 2002, with the same conditions existing as they still are today, Zender Environmental conducted a retrospective study in four villages and found that people who visited their dump were 2 to almost 4 times more likely to experience faintness, fever, vomiting, stomach pain, ear and eye irritation, headache, and/or numbness (Gilbreath, Zender & Kass, n.d.). The more often people visited the dump, the more likely they were to experience the symptoms. In a 2006 study by Gilbreath and Kass, Alaska Native Village dump sites without a way to separate and backhaul their hazardous wastes were found to present increased risks for lower birth weight, shorter gestation, and 4.3 times greater risk for several types of birth defects. It should be noted that multiple states across the country permit unlined construction and demolition (C &D) landfills under RCRA. These C & D landfills are nearly always in rural areas, where the vast bulk of tribes reside. Further, checkerboard jurisdiction on reservations means that open dumping by contractors and the general public occurs regularly.	Y	N	N	N	N	N	N	N	N	N	N			
119	NTTC	1	PESS, Exposure	N/A	In tribal communities and in rural and low-income communities across the country, citizens are recycling and recovering consumer products, like removing useable parts from dead vehicles, taking home the free sofa outside the landfill fence, fishing in the dikes and ditches. A study that could be potentially used as a surrogate for these types of activities was conducted by Athanasiadou, Cuadra, Marsh, Bergman, & Jakobsson (2008) where they looked at exposure to PBDEs and bioaccumulative hydroxylated PBDE metabolites in young people, including children, from Managua, Nicaragua. [abstract from Athanasiadou et al] Stephenson and Harrad published their critical review of BFRs emissions from waste soft furnishings in 2014 which contained their noteworthy recommendation that waste soft furnishings be treated with the same concern as e-waste containing BFRs. [excerpt from Stephenson and Harrad]	Y	N	N	N	N	N	N	N	N	N	N			
120	NTTC	1	PESS, Exposure	N/A	Leachate from Unlined Landfills. Waterborne –In rural areas, wastewater may go through primary treatment only, then is discharged to surrounding water bodies. But a wide range of chemicals has been found even in secondary treatment of wastewater from urban POTW's. Only in the last five years or less, have the number and type of chemicals being sampled expanded to include a wider range of chemicals of concern. [summaries regarding determination of various chemicals found in wastewaters from various locations]	Y	N	N	N	N	N	N	N	N	N	N			
121	NTTC	1	PESS, Exposure	N/A	Air Emissions from Open Waste Burning. This study investigated the occurrence of polychlorinated biphenyls (PCBs), and several additive brominated flame retardants (BFRs) in indoor dust and air from two Vietnamese informal e-waste recycling sites (EWRSs) and an urban site in order to assess the relevance of these media for human exposure (Tue et al. 2013). 50 The levels of PBDEs, HBCD, 1,2-bis-(2,4,6-tribromophenoxy)ethane (BTBPE) and decabromodiphenyl ethane (DBDPE) in settled house dust from the EWRSs (130-12,000, 5.4-400, 5.2-620 and 31-1400 ng g(-1), respectively) were significantly higher than in urban house dust but the levels of PCBs (4.8-320 ng g(-1)) were not higher. The levels of PCBs and PBDEs in air at e-waste recycling houses (1000-1800 and 620-720 pg m(-3), respectively), determined using passive sampling, were also higher compared with non-e-waste houses. The composition of BFRs in EWRS samples suggests the influence from high-temperature processes and occurrence of waste materials containing older BFR formulations. Results of daily intake estimation for e-waste recycling workers are in good agreement with the accumulation patterns previously observed in human milk and indicate that dust ingestion contributes a large portion of the PBDE intake (60%-88%), and air inhalation to the low-chlorinated PCB intake (>80% for triCBs) due to their high levels in dust and air, respectively.	Y	N	N	N	N	Y	N	N	N	N	N			
122	NTTC	1	PESS, Exposure	N/A	Further investigation of both indoor dust and air as the exposure media for other ewaste recycling-related contaminants and assessment of health risk associated with exposure to these contaminant mixtures is necessary.	Y	N	N	N	N	N	N	N	N	N	N			

123	NTTC	1	PESS, Exposure	N/A	The open burning of waste, whether at individual residences, businesses, or dump sites, is a large source of air pollutants (Wiedinmyer, Yokelson, & Gullett, 2014). These emissions, however, are not included in many current emission inventories used for chemistry and climate modeling applications. This paper presented the first comprehensive and consistent estimates of the global emissions of greenhouse gases, particulate matter, reactive trace gases, and toxic compounds from open waste burning. Global emissions of CO2 from open waste burning are relatively small compared to total anthropogenic CO2; however, regional CO2 emissions, particularly in many developing countries in Asia and Africa, are substantial. Further, emissions of reactive trace gases and particulate matter from open waste burning are more significant on regional scales. For example, the emissions of PM10 from open domestic waste burning in China is equivalent to 22% of China's total reported anthropogenic PM10 emissions. The results of the emissions model presented here suggest that emissions of many air pollutants are significantly underestimated in current inventories because open waste burning is not included, consistent with studies that compare model results with available observations.	Y	N	N	N	N	N	N	N	N	N	N	N			
124	NTTC	1	General, Exposure	N/A	Disposal pathway regardless must be considered because contamination of media occurs even with best practice and facilities.	Y	N	N	N	N	N	N	N	N	N	N	N			
125	NTTC	1	General, Exposure	N/A	Throughout Asia, non-PBDE BFRs like HBCD, have extensively polluted coastal waters (Isobe, Ogawa, Ramu, Sudaryanto, & Tanabe 2012). They used mussels as a bioindicator, as did studies by the US National Oceanic & Atmospheric Administration of coastal US waters (Isobe et al., 2012), Isobe et al were studying the presence of BFRs, the range throughout Asia, and the levels of concentrations. Among the three HBCD diastereoisomers, α-HBCD was the dominant isomer followed by γ- and β-HBCDs. Concentrations of HBCDs and DBDPE in mussels from Japan and Korea were higher compared to those from the other Asian countries, indicating extensive usage of these non-PBDE BFRs in Japan and Korea. Higher levels of HBCDs and DBDPE than PBDEs were detected in some mussel samples from Japan. The results suggest that environmental pollution by non-PBDE BFRs, especially HBCDs in Japan, is ubiquitous. This study provides baseline information on the contamination status of these non-PBDE BFRs in the coastal waters of Asia. More than 1,500 construction and demolition debris (CDD) landfills operate in the United States (U.S.), and U.S. federal regulations do not require containment features such as low-permeability liners and leachate collection systems for these facilities (Powell, Jain, Smith, Townsend, & Tolaymatl; 2015). Here we evaluate groundwater quality from samples collected in groundwater monitoring networks at 91 unlined, permitted CDD landfills in Florida, U.S. A total of 460,504 groundwater sample results were analyzed, with a median of 10 years of quarterly or semiannual monitoring data per site including more than 400 different chemical constituents. Downgradient concentrations of total dissolved solids, sulfate, chloride, iron, ammonia-nitrogen, and aluminum were greater than upgradient concentrations ($p < 0.05$). At downgradient wells where sulfate concentrations were greater than 150 mg/L (approximately 10% of the maximum dissolved sulfate concentration in water, which suggests the presence of leachate from the landfill), iron and arsenic were detected in 91% and 43% of samples, with median concentrations of 1,900 µg/L and 11 µg/L, respectively. These results show that although health-based standards can be exceeded at unlined CDD landfills, the magnitude of detected chemical concentrations is generally small and reflective of leached minerals from components (wood, concrete, and gypsum drywall) that comprise the bulk of discarded CDD by mass.	N	N	N	N	N	Y	N	N	N	N	N			
126	NTTC	1	Human Health	N/A	Prior to the Lautenberg Act amending TSCA, risk assessments have not accounted for existing body burden suite of chemicals, which is also not addressed in either the Human Health Risk Assessment Guidelines nor the Cumulative Risk Guidelines listed on the EPA web sites. Tribal people are especially exposed to larger volumes of chemicals due to their tribal lifeways and their geographic locations in relation to manufacturing and pollutant deposition. Along with higher amounts of toxin exposure and bioaccumulation, there is greater risk of the suite of chemicals interacting and causing health effects not accounted for by single-chemical risk assessments. NTTC continues to urge EPA to move beyond just cancer risk or only toxicity, and assess more concerning endocrine disrupting health effects as levels of risk from known endocrine disrupter chemicals (EDCs). These EDCs are particularly dangerous and not adequately assessed in the most recent risk scenarios.	Y	N	N	N	N	N	N	N	N	N	N			
127	NTTC	1	General	N/A	In August 2015, EPA published for public comment its TSCA Work Plan Chemical problem formulation and initial assessment documents for the three flame retardant clusters Brominated Bisphenol A (TBBPA), Chlorinated Phosphate Esters (CPE), and Cyclic Aliphatic Bromides (HBCD) (USEPA 2015c). In response NTTC provided written comments to that docket which we recapture here in relevance to problem formulation and risk evaluation under the amended TSCA.	N	N	N	N	N	N	Y	N	N	N	N			
128	NTTC	1	General, Exposure	N/A	NTTC appreciates EPA's inclusion of fish consumption by subsistence fishers and their children when evaluating exposure pathways for CPE. We specifically highlight EPA's commitment to account for the high-end fish consumption of subsistence fishers—including pregnant women, children and adults—the majority of whom are the tribal population.	N	N	N	N	N	N	Y	N	N	N	N			
129	NTTC	1	Human Health	N/A	NTTC agrees with the need to evaluate the hazard endpoints that go beyond cancer risk and include target organ effects, reproductive and developmental effects, and neurotoxicity (U.S. EPA 2015d, p. 32, 34).	N	N	N	N	N	N	Y	N	N	N	N			
130	NTTC	1	Human Health, Exposure	N/A	In CPE Problem Formulation of 2015, EPA stated it would exclude from further assessment the exposures of birds, terrestrial wildlife, or sediment-dwelling organisms as well as food other than fish. In our comments, NTTC noted its disagreement with EPA's decision as these exclusions fail to account for the subsistence diets of tribal populations, which include these species and other resources that consume these species. In the CPE Problem Formulation, EPA noted that [m]onitoring studies have reported the detection of TCEP in aquatic species, mammalian species, herring gull eggs and pine needles. …these materials are likely bioavailable and could be observed in a biological matrix." (U.S. EPA 2015d, p. 22). The referenced studies showed detection of CPEs in the breast milk of women in Sweden, Asia, Japan, the Philippines, and Vietnam. These data demonstrate the need for consideration of the natural environment and food resources of tribal populations. Aquatic species, mammalian species and gull eggs are all natural resources upon which tribal populations subsist.	N	N	N	N	N	N	Y	N	N	N	N			

131	NTTC	1	Fate, Exposure	N/A	Yu et al. (2016) compiled and reviewed existing literature on the contamination status of BFRs in abiotic and biotic environments in China, including polybrominated diphenyl ethers (PBDEs), hexabromocyclododecane, tetrabromobisphenol A and new BFRs. 58 Temporal trends were also summarized and evaluated. Based on this review, it has been concluded that (1) high concentrations of PBDEs were generally related to the e-waste disposal processing, while the spatial distribution pattern of other BFRs was not necessarily in accordance with this; (2) extremely high concentrations of BFRs in indoor dust emphasized the importance of indoor contamination to human body burdens, while more work need to be done to confirm its contribution; (3) PBDEs in electronics dismantling workers were higher compared to the general population, indicating the occupational exposure should be of particular concern; (4) more data are now becoming available for BFRs in aquatic and terrestrial organisms not previously studied, while studies that consider the occurrence of BFRs in organisms of different trophic levels are still of urgent need for evaluating the fate of BFRs in the food web; and (5) limited data showed a decreasing trend for PBDEs, while more data on time trends of BFR contamination in various matrices and locations are still needed before the impact of regulation of BFRs can be assessed.	N	N	N	N	N	N	Y	N	N	N	N			
132	NTTC	1	PESS, Exposure	N/A	During problem formulation of HBCD, EPA identified inhalation, dermal and lifetime exposure assessments as data gaps that add uncertainty to EPA's risk assessment of HBCD. NTTC continues to maintain that EPA must include tribal populations in its plans to "conduct additional risk analysis on potential worker, general population, consumer and environmental exposures under the TSCA Existing Chemicals Program" (U.S. EPA, 2015e, p. 11).	N	N	N	N	N	N	Y	N	N	N	N			
133	NTTC	1	PESS, Exposure	N/A	EPA noted that HBCD is a persistent pollutant in environmental media, expected to occur primarily as particulates, which may undergo long range transport, and is highly bioaccumulative with measured fish Bioconcentration factor values of greater than 18,000 (U.S. EPA, 2015e, p. 22). Given this, EPA must consider the impact of consumption by tribal citizens who live in geographic ranges where the majority of industrial-sourced particulates are deposited, who rely on traditional foods of fish and marine mammals which bioaccumulate toxins via fish and algae consumption. Further, on page 24 of the HBCD Problem Formulation, EPA referenced data of HBCD measured in the blubber and liver of various marine mammals; both of these tissues are a staple, consumed in large quantities, in Arctic tribal citizens' diets (U.S. EPA, 2015e, p. 76). Then, regarding bioaccumulation, EPA referenced studies that note the widespread detection and high levels of HBCD in aquatic and terrestrial organisms: invertebrates, fish, birds and their eggs, and marine mammals, all of which are traditional food resources of tribes. Finally, HBCD was detected in breast milk, adipose tissue, blood, and both maternal and umbilical serum (U.S. EPA, 2015e, p. 85). These references to EPA's own work highlights NTTC's principle that EPA must account for tribal populations, especially sensitive infant and child populations, in its risk evaluation of HBCD.	N	N	N	N	N	N	Y	N	N	N	N			
134	NTTC	1	PESS, Exposure	N/A	NTTC supports the EPA's decision for comprehensive studies for many endpoints for all cluster members of the TBB/TBPH cluster. NTTC also supports the EPA's statement of need for comprehensive studies on bioaccumulation of all brominated phthalate cluster (BPC) chemicals. Considering persistence and toxicity data on other brominated flame retardants, bioaccumulation and persistence data are extremely necessary. With the potential for acute and chronic toxicity, reproductive toxicity, and negative health effects on fetal development and endocrine disruption, it is alarming that the U.S. allows continued use of BPC chemicals. NTTC maintains its position that EPA must also consider chemical body burden, in addition to testing all cluster members individually and quantifying major degradation products. With suggested potential of long-term exposure of TBB/TBPH to wildlife, EPA stated that "chronic testing is recommended to address those organisms likely exposed in order to characterize potential population level effects"; and that suggested potential of "exposure and uptake by organisms present in water bodies including aquatic plants thus, hazard and bioaccumulation characterization is needed for these organisms" (U.S. EPA, 2015f, p. 39).60 (TBB/TBPH PF and DNA, 08/158, pp. 39) Therefore, NTTC reiterates that EPA must then also consider the effect of subsistence foods and traditional natural resources on the tribal population. This includes high-level consumption of marine mammals, such as whale, seal, walrus, and sea lion; fish and shellfish, such as salmon, herring, halibut, crab, and mussels; avian species such as duck, geese, and gull; and wildlife such as moose, deer, caribou, and elk.	N	N	N	N	N	N	Y	N	N	N	N			
135	NTTC	1	Exposure	N/A	Since the problem formulations noted above were released in 2015, NTTC has further researched these chemicals in commerce. Brominated flame retardants are found to be a frequent and at times high concentration of indoor dust in houses, apartments, daycare centers, and primary schools, and of the highest concentrations in North America and Europe (Malliari & Kalantzi, 2017). 61 "Results from the studies showed that dust ingestion was the dominant exposure pathway for most studied BFRs compared to indoor air inhalation and dermal contact, especially for infants and toddlers who have higher exposures than older children."	N	N	N	N	N	N	Y	N	N	N	N			
136	NTTC	1	Human Health	N/A	HBCD Toxicity testing has detected reproductive, developmental and behavioral effects in animals where exposures are sufficient (Marvin et al. 2011). Recent toxicological advances include a better mechanistic understanding of how HBCD can interfere with the hypothalamicpituitary-thyroid axis, affect normal development, and impact the central nervous system defects.	N	N	N	N	N	N	Y	N	N	N	N			
137	NTTC	1	Human Health, Exposure	N/A	Fish represents source of nutrients and major dietary vehicle of lipophilic persistent contaminants (Maranghi 2013). The study compared the effects of two legacy and two emerging fish pollutants (Hexabromocyclododecane HBCD; 2,2',4,4'-Tetrabromodiphenyl ether BDE-47; 2,2',4,4',5,5'-Hexachlorobiphenyl PCB-153; 2,3,7,8-Tetrachlorodibenzo-p-doxin TCDD) in juvenile female mice exposed through a salmon based rodent diet for 28 days (dietary doses: HBCD 199 mg/kg bw/day; BDE-47 450 µg/kg bw/day; PCB-153 195 µg/kg bw/day; TCDD 90 ng/kg bw/day). Dose levels were comparable to previously reported developmental Lowest Observed Adverse Effect Levels. None of the treatments elicited signs of overt toxicity, but HBCD increased relative liver weight. All compounds caused changes in liver, thymus and thyroid; spleen was affected by BDE-47 and PCB-153; no effects were seen in uterus and adrenals. Strongest effects in thyroid follicles were elicited by PCB-153, in thymus and liver by BDE-47. HBCD and BDE-47 induced liver fatty changes, but appeared to be less potent in the other tissues. HBCD, BDE-47 and TCDD increased serum testosterone levels and the testosterone/estradiol ratio, suggesting a potential involvement of pathways related to sex steroid biosynthesis and/or metabolism. The results support the role of toxicological studies on juvenile rodents in the hazard characterization of chemicals, due to endocrine and/or immune effects.	N	N	N	N	N	N	Y	N	N	N	N			

138	NTTC	1	PESS, Exposure	N/A	Tribal people's socioeconomic status and customary lifeways support a representative subpopulation role. Some aspects of Tribal people's lifestyle are shared by non-Tribal peoples living in the same or similar geographic area, and/or of similar socio-economic levels. These lifestyle aspects are not necessarily traditional in the sense of purposeful transfer between generations, and they often do not have the same weight of value, or a negative value. But their characteristics are still critical to ensure that risk assessments are relevant to tribal peoples. By making profiles that reflect these aspects of Tribal people's lifestyle, risks of other subgroups that also were not represented can be more accurately assessed as well. The standard of relevance dictates that the risk assessment models used are applicable to the population being examined. As noted above, tribal lifeways result in people interacting with and consuming resources from the ecological environment more frequently and in greater volumes than the general population, and in some cases, what would orders of magnitude differences.	Y	N	N	N	N	N	N	N	N	N	N			
139	NTTC	1	Fate, PESS, Exposure	N/A	Extensive research indicates significantly concerning characteristics of brominated flame retardants (BFRs). -BFRs are extensively present in environmental and biota samples worldwide, -BFRs are persistent, bioaccumulative, and biomagnified, and -BFRs have high potential toxicity to both ecological environment and human health. Thus BFRs have an even greater potential toxicity to those who more frequently interact with and consume resources from the ecological environment. This is supported by Yu et al. (2016), Wang et al. (2010).	N	N	N	N	N	N	Y	N	N	N	N			
140	NTTC	1	Fate, PESS, Exposure	N/A	The particular relevance to tribal lifeways as representative of potentially exposed and susceptible subpopulations is especially demonstrated in Yu et al (2016) who, just two years ago, published their review of then existing literature on the contamination status of BFRs in abiotic and biotic environments in China, including polybrominated diphenyl ethers (PBDEs), HBCD, tetrabromobisphenol A (TBBPA), and newer brominated flame retardants (BFRs). Temporal trends were also summarized and evaluated. They concluded that (1) high concentrations of PBDEs were generally related to the e-waste disposal processing, while the spatial distribution pattern of other BFRs was not necessarily in accordance with this; (2) extremely high concentrations of BFRs in indoor dust emphasized the importance of indoor contamination to human body burdens, while more work need to be done to confirm its contribution;(3) PBDEs in electronics dismantling workers were higher compared to the general population, indicating the occupational exposure should be of particular concern; (4) more data are now becoming available for BFRs in aquatic and terrestrial organisms not previously studied, while studies that consider the occurrence of BFRs in organisms of different trophic levels are still of urgent need for evaluating the fate of BFRs in the food web; and (5) limited data showed a decreasing trend for PBDEs, while more data on time trends of BFR contamination in various matrices and locations are still needed before the impact of regulation of BFRs can be assessed.	N	N	N	N	N	N	Y	N	N	N	N			
141	NTTC	1	Fate, PESS, Exposure	N/A	The findings by Wang et al. (2010) are alarming when considered in relation to tribal lifeways and the disposal of electronics in unlined landfills or dumpsites and by open burning. Brominated flame retardants (BFRs) in house dust from the electronic waste (ewaste) recycling and urban areas of South China showed that PBDE levels were comparable to the values found in North America. ...The distinct dust BFR profiles observed in the two studied areas were reflective of activities in these areas (electronics industry vs. e-waste recycling). The estimated daily intakes (EDIs) via house dust were much higher than those via other indoor pathways (air, fish, human milk, and toys). Despite the potentially low deleterious risk of PBDE exposure via house dust as suggested by the hazard quotients, this exposure pathway should be of great concern because of the higher BFR exposures for children and the presence of other BFRs (such as DBDPE) which have not yet been fully investigated. Housing-related exposures, for example. Used furniture and other items containing flame retardants, are gifted to others, purchased at thrift stores or yard sales, and found as free items on sidewalks, roadsides, and at the landfill. Furniture is kept longer than in urban and general populations, often well-passed typical time ranges and simply covered with sheets, blankets or other fabrics. Housing structures are older and smaller, similar to low-income and rural areas, and do not contain air conditioning systems, do not contain air filters, and residents rely on open windows and doors for summer cooling and for venting when cooking and cleaning. Dusting and vacuuming equipment is typically older, lesser quality, or non-existent. Inhalation and ingestion are major exposure pathways and EPA must account for these situations and factors when considering risk.	N	N	N	N	N	N	Y	N	N	N	N			
142	NTTC	1	Fate, PESS, Exposure	N/A	Public infrastructure: The tribal communities we discuss live with significantly outdated public infrastructure, e.g., private wells for drinking water, unplumbed homes, open dumping, kids playing around open dumps. They and others in rural America experience lifestyles much different from the urban centers: recreational swimming in natural water bodies, produce gardening and farming, living near open dumping, unpaved road dust, Arctic entry ways, living all or most of lifetime where they were raised, potlucks and social gatherings, sharing of harvested, grown, and gathered foods. For rural Alaska villages, drinking water, showers, and laundry are accessed at the public watering point, often called the washeteria, where wastewater is handled with only primary treatment. Schreder & La Guardia (2014) studied levels of flame retardants in residential house dust and laundry wastewater as a transport pathway from homes to the outdoor environment in communities near the Columbia River in Washington state (WA), accounting for influent and effluent from two wastewater treatment plants (WWTPs) servicing these communities. Of the 21 brominated and chlorinated compounds, including HBCD, detected in dust, 18 were also detected in laundry wastewater. Comparison of flame retardant levels in WWTP influents to estimates based on laundry wastewater levels indicated that laundry wastewater may be the primary source to these WWTPs.	N	N	N	N	N	N	Y	N	N	N	N			

143	NTTC	1	Fate, PESS, Exposure	N/A	Lack of options in lifestyle. Food is gathered from land and waters locally and regionally. In the 2014 analysis update on subsistence in Alaska, rural residents harvested between 145 and 405 pounds per person per year of wild foods (Fall & Wolfe, 2016).67 The average per person per year amount was about 275 pounds for rural residents versus 19 for urban residents. That was about 0.75 pounds a day per person for rural residents versus 0.05 for urban residents. Costs of store items in Alaska villages and rural areas is prohibitive, often four or more times more expensive than in urban areas, so in general, there are less alternatives to food gathered. There are significantly fewer employment opportunities and higher costs for heating fuel, vehicle fuel, and household basic necessities due to added on cost of shipping items to village. Without incorporating these general profiles, the proposed problem formulations are not relevant to Tribal peoples, a susceptible subpopulation. La Guardia, Hale, Harvey, Mainor, Ciparis (2012) studied in-situ accumulation of HBCD, PBDEs, and several alternative flame-retardants in the bivalve and gastropod. While they found that several alternative brominated flameretardants (BFRs) were being detected in the environment, they noted that contaminant bioavailability is influenced by the organisms' ecology (i.e., route of uptake) and in situ environmental factors. We observed that the filter-feeding bivalve (Corbicula fluminea) and grazing gastropod (Elimia proxima), collected downstream from a textile manufacturing outfall. Maximum levels of total hexabromocyclododecane diastereomers (ΣHBCDs) and those of polybrominated diphenyl ethers (ΣPBDEs) were among the highest reported to date worldwide. While BDE-209 was once thought to be nonbioavailable and resistant to degradation, it was the dominant BFR present and likely debromination products were detected. Contributions of α- and β-HBCD were higher in tissues than sediments, consistent with γ-HBCD bioisomerization. Mollusk bioaccumulation factors were similar between HBCD and PBDEs with 4 to 6 bromines, but factors for TBB, TBPH, and BTBPE were lower. Despite different feeding strategies, the bivalves and gastropods exhibited similar BFR water and sediment accumulation factors.	N	N	N	N	N	N	Y	N	N	N	N			
144	NTTC	1	Fate, PESS, Exposure	N/A	In consideration of BFRs effect on flora, for example, Wu, Huang & Zhang (2016) investigation of the accumulation and phytotoxicity of technical hexabromocyclododecane (HBCD) in maize, using young seedlings exposed to solutions of technical HBCD at different concentrations. The results demonstrate HBCD accumulation in both the roots and shoots of the plant, HBCD causing DNA damage, and variances between HBCD diastereoisomers. The uptake kinetics showed that the HBCD concentration reached an apparent equilibrium within 96hr, and the accumulation was much higher in roots than in shoots. HBCD accumulation in maize had a positive linear correlation with the exposure concentration. The accumulation of different diastereoisomers followed the order γ-HBCD>β-HBCD>α-HBCD. Compared with their proportions in the technical HBCD exposure solution, the diastereoisomer contribution increased for β-HBCD and decreased for γ-HBCD in both maize roots and shoots with exposure time, whereas the contribution of α-HBCD increased in roots and decreased in shoots throughout the experimental period. These results suggest the diastereomer-specific accumulation and translocation of HBCD in maize. Inhibitory effects of HBCD on the early development of maize followed the order of germination rate>root biomass≥root elongation>shoot biomass≥shoot elongation. Hydroxyl radical (OH) and histone H2AX phosphorylation (γ-H2AX) were induced in maize by HBCD exposure, indicative of the generation of oxidative stress and DNA double-strand breaks in maize. An OH scavenger inhibited the expression of γ-H2AX foci in both maize roots and shoots, which suggests the involvement of OH generation in the HBCD-induced DNA damage. The results of this study will offer useful information for a more comprehensive assessment of the environmental behavior and toxicity of technical HBCD.	N	N	N	N	N	N	Y	N	N	N	N			
145	NTTC	1	Fate, PESS, Exposure	N/A	Several studies in the last few years have built on data analysis of BFRs in aquatic and terrestrial species. Sun et al. (2018) measured α-, β-, and γ-HBCDs in three freshwater fish—mud carp, tilapia, and plecostomus—from rivers and an electronic waste (ewaste) recycling site in Pearl River Delta, South China. [Summaries from mutliple studies]	N	N	N	N	N	N	Y	N	N	N	N			
146	NTTC	1	General, PESS, Exposure	N/A	With Tribes as a representative population for greater environmental media exposure risk, any resultant action levels will not only protect tribes and the general population, but the ethnic, minority, and rural population groups that may be at higher risk due to their customary lifestyle and activities and/or traditional practices. Fishing illustrates this point. Fishing is a universal practice for Alaska Tribes, potential exposure via ingestion of contaminated fish is higher due to higher consumption, as is potential exposure via inhalation through smoking fish, and other heat preparation methods particularly with poor indoor ventilation, via potential absorption when fishing and preparing a greater amount of fish, via non-dilution of contaminated fish with fish from another location due to unavailability of store-bought fish, via particular practices associated with fishing, which may include gathering greens and using untreated water near the fishing spot, etc. Also, the full Tribal population – from infant to elder, disabled, single parents with small children and relative living outside the village – is exposed due to sharing of fish. This is a magnified representation of the Alaska population as a whole, particularly the rural population, which tend to fish for, and share and eat fish like salmon, at a much greater rate than their counterparts in the contiguous states. The same can be said for exposure to contaminated “game meats”, marine mammals, berries, water and other environment sources due to customary food resources and recreational activities. With Tribes as representative, the full Alaska population is protected.	Y	N	N	N	N	N	N	N	N	N	N			
147	NTTC	1	General, PESS, Human Health	N/A	The sociocultural consequences to Tribal communities of overexposure to chemicals are as significant, or more significant, compared to the consequences to other groups. The small population size, high-context, and group-oriented nature of Tribal populations translates to substantial impact on health and well-being when a Tribal member is negatively affected by chemical exposures. For example elders are a significant resource in their community and fill multiple roles. Teachers of cultural values and mores for their community including other older adults that are younger than the elder in addition to children and teens. It is well documented that tribal people’s socio-cultural knowledge base is more internalized and is not adequately learned via verbal or written instructions. It must be acquired over a lifetime of experiencing the day-to-day contexts of being a tribal person and relating with elders that have fully acquired the knowledge in their time by being with generations past. Sources of historical information shared with their community including other older adults that are younger than the elder in addition to children and teens. Leaders whose experience provides stability and experience to the tribal council and in consultations with government agencies. Caretakers for extended family members, providing unpaid childcare. A grandmother who develops cancer will not be able to care for her grandchildren, parents may miss work resulting in job or income loss, or children may miss a critical mentor role or be injured because they are left alone.	Y	N	N	N	N	N	N	N	N	N	N			
148	NTTC	1	General, PESS, Human Health	N/A	Impacts to societal health and well-being contribute to disproportionate health and socioeconomic indicators. E.g., exposure to a certain chemical affects childhood brain development, causing neuro-developmental delays, which are compounded as the child progresses through school and Tribal populations suffer from low high school and college graduation rates.	Y	N	N	N	N	N	N	N	N	N	N			

149	NTTC	1	General, PESS, Exposure	N/A	While NTTC recognizes that part of EPA's risk assessment process is collecting existing data on the chemicals in question, asking tribes to fill this data gap is unreasonable. EPA must provide funding before starting the process (at least more than one year prior) to request tribes gather information. Specifically, sampling within tribal homes in high-risk areas would provide valuable data to further complete risk assessments accounting for high-risk, vulnerable tribal populations. EPA must take into account widespread backyard open burning and open burning at both municipal and construction & demolition landfills. Tribal and other rural citizens are exposed to chemicals in commerce via this pathway, including HBCD. These types of burning are prevalent in underserved tribal communities on reservations in the U.S. and other rural lands, including nearly every community in the State of Alaska. These communities rarely have proper burn units nor appropriate safety protocols to prevent residents' inhalation.	Y	N	N	N	N	N	N	N	N	N	N	N			
150	NTTC	1	General, PESS, Exposure	N/A	Again, regarding fish consumption and the rate referenced above, in relation to population scenarios, the tribal population scenario is the most appropriate to use for risk assessments by EPA, because their rules indicate that they are to protect the population of highest risk. As identified in the 2015 problem formulation for the HBCD cluster, EPA must use fish consumption rates for subsistence fishers in aggregate exposure for those who rely heavily on locally sourced fish.	Y	N	N	N	N	N	N	N	N	N	N	N			
151	NTTC	1	General, PESS, Exposure	N/A	It is imperative that EPA consider potential cumulative exposure—including multiple chemical exposure—in these risk assessments because it is an on-going void in implementing environmental justice policies. This is a significant problem that EPA is not considering cumulative exposure in the risk assessment process at this time. It is an environmental justice issue affecting tribes, who rely heavily on high volumes of fish and aquatic mammals for half or more of their diet. Additionally, a large percentage of American Indian and Alaska Native communities are at or below the poverty level. This translates to lower replacement cycles of furniture, toys, clothing etc. from those with higher toxicities to more recently manufactured items of lower toxicities. For example, although PCB is no longer manufactured, studies have detected it in Puget Sound tissue sample monitoring. EPA must also look at wastewater outside of only the Toxics Release Inventory, which does not account for small local government facilities like unlined but permitted landfills, unpermitted landfills, open dumps, and open dump and backyard burning. As the Council has previously discussed with EPA, the stovepiped processes of EPA fails in protecting tribes from exposures to chemical in commerce.	Y	N	N	N	N	N	N	N	N	N	N	N			
152	NTTC	1	PESS, Exposure	N/A	Most states have developed fish consumption advisories to protect residents from toxins in fish species known to bioaccumulate contaminants. One particular challenge that has been expressed by state fish advisory programs is communicating fish advisory information to ethnic or immigrant populations who do not speak English and are difficult to reach via fish advisory communication methods targeted toward the broader public. Ethnic or immigrant populations are specifically at risk due to their predominantly urban fishing locations that of contaminants than species typically consumed by sport fisherman (due to benthic feeding habits or tolerance to live in polluted waters). EPA maintains a compendium of fish advisory technical information including contacts for state and Tribal fish consumption advisory programs managers at its website at https://www.epa.gov/fishtech. In addition, EPA supports a fish advisory program manager listserv to promote sharing of fish consumption advisory technical information among state and Tribal fish advisory program managers and EPA. The EPA contact for this program is Sharon Frey (Frey.Sharon@epa.gov or 202-566-1480) and she should be contacted to assist with compiling existing consumption and exposure information for ethnic or immigrant subsistence fishers residing in urban areas.	Y	N	N	N	N	N	N	N	N	N	N	N			

Problem Formulation Documents - Public Comments

GENERAL COMMENTS- APPLY TO ALL

#	Submitter	Attachments (#)	Category	Document Section #
1	ACC	3	General	N/A
2	ACC	3	General	N/A
3	ACC	3	General	N/A
4	ACC	3	General	N/A

Comment
Section 26 of TSCA mandates that EPA make science-based decisions under Sections 4, 5, and 6 of TSCA in a manner consistent with the best available science and the weight of the scientific evidence. EPA's development of a structured process to identify, evaluate, and integrate evidence from both the hazard and exposure assessments developed during the TSCA risk evaluations is appropriate and will provide increased transparency into the TSCA risk evaluation process.
In general, EPA should make the results of its systematic review process available as part of the docket for each risk evaluation, including its selection of key studies and study quality evaluations.
EPA has identified those conditions of use that will be within the scope of the risk evaluations, as well as those that will be excluded. The risk evaluation rule makes clear that EPA should focus on those conditions of use that raise the greatest potential for risk. ACC generally supports the approach taken to addressing conditions of use within each of the 10 problem formulations. This approach allows EPA to be efficient, while still addressing the highest priority conditions of use that pose the greatest potential risk.
The problem formulation documents present a thoughtful approach to identifying current uses that are appropriate for inclusion within the scope of the risk evaluation. We also appreciate EPA's efforts to explain why the conditions of use that are not within scope will be excluded. ACC encourages continued stakeholder engagement with manufacturers and users of these chemicals throughout the risk evaluation process to ensure the best available information is used.

Applies to ALL (Y/N)	RAD POC	Docket #	Action Needed
Y			
Y			
Y			
Y			

5	ACC	3	General	N/A
6	ACC	3	General	N/A

As EPA gains more experience conducting TSCA risk evaluations for high priority chemicals, it would be useful if the Agency would develop a framework that articulates its process for deciding when conditions of use are in or out of scope. This would help EPA streamline future efforts, provide greater public understanding of EPA's decisions, increase transparency and reproducibility, and enable industry to identify the types of information that may be most helpful for manufacturers, processors, and downstream users to develop and/or share with EPA. Developing a framework would also help industry anticipate which conditions of use will be the likely focus in future assessments so that they can direct resources efficiently to develop and/or gather information relevant to EPA's potential risk evaluations and facilitate proactive data collection efforts.

"Section 9(d) of TSCA imposes a general requirement on EPA to consult and coordinate with other federal agencies for purposes of "achieving the maximum enforcement" of TSCA while imposing the "least burdens of duplicative requirements on those [subject to TSCA]." This Section 9(d) coordination requirement has existed since TSCA was originally enacted and was unchanged by the 2016 amendments. Section 9(d) is a general policy directive that applies to EPA for all TSCA implementation activities. The risk evaluation rule also contains a general consultation provision that codifies the statutory requirement for interagency collaboration during the risk evaluation process." The principle driving this coordination requirement is that EPA should avoid imposing unnecessary or duplicative burdens on regulated entities and avoid regulatory actions best taken by another agency or under other EPA authority. This necessarily includes all manner of Agency interaction with regulated entities, including submission of information, docket management, responses to comments, and other engagement with multiple regulatory bodies. Where non-TSCA regulatory schemes are sufficiently effective at addressing risk, EPA may properly exclude covered conditions of use from the scope of the risk evaluation.

Y			
Y			

7	ACC	3	Exposure	N/A
8	ACC	3	Exposure	N/A
9	ACC	3	General	N/A
10	ACC	3	Exposure	N/A

Regarding occupational exposures, EPA should consult early with OSHA in the risk evaluation process—certainly at the earliest stages of the risk evaluation and well before the scope is released. This consultation should continue throughout the risk evaluation. None of the 10 problem formulations make clear what consultation may have occurred, or when it occurred. Although the problem formulations do identify available occupational exposure levels (OELs), i.e., PELs, TLVs, and IDLH values, additional information should be provided regarding the factors EPA will take into consideration when evaluating OELs. For example, consideration should be given to whether the OEL includes current toxicological and epidemiological data to support the development of the threshold limit value. EPA also presents summarized personal monitoring air samples obtained from OSHA inspections, but it is not clear how these data were obtained from OSHA and under what circumstances the data were gathered.
EPA should give preference to direct data obtained for uses being evaluated with consideration given to how the data were gathered (i.e., workplace exposure monitoring data are gathered on a more routine basis while OSHA monitoring is conducted typically in compliance with the OSHA Technical Manual for 8 hours and the sample will generally involve the scenario or tasks in which the highest exposure is expected).
For purposes of 9(d) compliance, it would be helpful if subsequent risk evaluation scopes offer more detail regarding EPA's coordination with other agencies, including information such as consultation plans, data shared, etc. We encourage EPA to include such a coordination plan in future scopes and to include these plans in the draft risk evaluations, including notations where consultation has occurred.
It would be helpful for EPA to describe the decision criteria/framework by which it will evaluate whether to include occupational exposures in the scope of a risk evaluation. This description was not included in the 10 problem formulation documents.

Y			
Y			
Y			
Y			

11	ACC	3	General	N/A
12	ACC	3	General	N/A

EPA should apply a tiered approach throughout the risk evaluation process–from screening/prioritizing chemicals to conducting risk evaluations–under amended TSCA. This is essential to enable EPA to meet TSCA's statutory deadlines for completing risk evaluations, adhere to TSCA's robust scientific standards, and enable both EPA and the regulated community to apply limited resources efficiently.
When a screening-level assessment is insufficient to conclude a lack of risk to exposed populations, EPA should take steps to refine the risk evaluation allowing more accurate quantification of potential risks. The scoping/problem formulation documents indicate where the EPA feels it has sufficient information and where additional information and use of higher-tier tools is warranted. In situations where EPA may need to perform higher-tier assessments for the risk evaluation, more information is needed on the types of data and techniques that EPA will utilize. For example, EPA should indicate how probabilistic risk assessment (PRA), uncertainty analyses, and the use of statistical tools such as Bayesian statistics would be used at a higher tier within the overall problem formulation framework. A tiered, iterative approach is critical to the production of high quality risk evaluations based on the best available information.

Y			
Y			

13	ACC	3	Exposure	N/A

The value of tiered exposure assessment is well-established. In its 1992 guidelines on exposure assessment,10 EPA discusses the value of tiered exposure assessments from screening-level assessments to more complex assessments. This perspective was reiterated in EPA's 2016 peer review draft update of the 1992 guidelines. The 2016 draft update included specific discussion of considerations in tiered assessments, as well as the notion of "fit for purpose" assessments, stating "[t]he type and purpose of an exposure assessment determine the data and information requirements." The EPA Office of Research and Development (ORD) ExpoBox tool box for exposure assessors identifies exposure assessments tools by tier and type, both screening-level and refined, for planning, scoping, and problem formulation. The purpose of tiered exposure approaches is well understood: to identify uses of chemicals that, under very conservative (e.g., maximum) exposure assessment assumptions, are not likely to pose a health risk. Depending on the conditions of use, the exposure assessment information can be used either to identify a chemical as a low priority or to be factored into the overall risk evaluation. Exposures that initially exceed hazard benchmarks in Tier-1 exposure assessments would require more refined, higher-tiered approaches to exposure assessments. This would include the application of more realistic parameters related to the likely duration, intensity, frequency, and number of exposures and more realistic exposure scenarios to more accurately quantify actual risks of the chemical. The importance of EPA using a tiered approach to exposure assessment in its TSCA risk evaluations cannot be overstated. A tiered approach allows for both a more rapid, yet systematic, approach for assessing conditions of use in a first-tier screen, so that resources are used effectively when a refined exposure assessment is necessary for those conditions of use that do not "pass" a first-tier screen. well-defined, tiered exposure approach can lead to greater efficiencies in chemical risk evaluations under TSCA. Congress clearly valued such efficiency highly as evidenced by the aggressive deadlines it set for EPA to conduct TSCA risk evaluations. Congress also directed the Agency to consider the likely duration, intensity, frequency, and number of exposures under the conditions of use.

Y			

14	ACC	3	Exposure	N/A

The value of tiered exposure approaches in risk evaluations is even broader than exposure assessment. This was discussed in the Health and Environmental Sciences Institute's (HESI) Coordinated Risk Assessment in the 21st Century (Risk21) project. A review article published in 2014 discussing Risk21's principles and framework for decision-making in human health risk assessment emphasizes that problem formulation for risk assessment should not be a hazard-driven process, but instead should start with exposure, focusing on exposure scenarios of greatest concern integrated with hazard information to support risk-based decision making. The article suggests this approach would result in an early estimate of potential human exposure in relevant populations, including susceptible populations, which would characterize the degree of specific toxicological data needs. The Risk21 framework also addresses two other principles: (1) additional data should be acquired "only if necessary and when they add value" and (2) flexibility, "such that a higher tier hazard assessment approach can be coupled with a lower tier exposure approach, and vice versa." Considerable progress has been made over the last several years in developing screening-level exposure prediction models for chemicals in commerce. These approaches can be of particular utility in conducting Tier-1 assessments for many chemicals. In the context of TSCA's risk evaluations, tiered-assessment concepts equip EPA with the tools it needs to meet TSCA's aggressive deadlines for completing risk evaluations of high priority chemicals. Tiered assessments also enable EPA to apply limited resources in an efficient manner. Using a clear, science-based tiered-assessment approach, EPA and the regulated community can perform exposure assessments in TSCA risk evaluations, enabling efficient decision-making.

Y			

15	ACC	3	Exposure	N/A
16	ACC	3	Exposure	N/A

The draft problem formulation documents of the initial 10 chemicals mention the Agency's plans to use tiered exposure assessments in its risk evaluations of these chemicals, but the documents lack specifics. A clear "road map" showing EPA's approach to tiered exposure assessments is needed in EPA's scoping documents. Such a road map—or decision tree—would provide structure to EPA's approach to exposure assessments under TSCA. This structure would also be useful to explain how EPA will integrate the results of its tiered exposure assessments with the results from its tiered-hazard assessments in TSCA risk evaluations. A road map would signal to the regulated community the type of reasonably available exposure information EPA plans to rely upon, what additional exposure information might be needed, and what actions manufacturers could take early in the risk evaluation process to provide EPA the needed exposure information. EPA should delineate what kinds of data and information it could accept to refine lower-tier exposure assessments.

Specifically, with respect to potential human exposures in the problem formulation documents, EPA should identify:
-The screening-level exposure information/models EPA will use to address human exposure in Tier-1 exposure assessments;
-The approach to hazard characterization and threshold EPA will use to ascertain the need for a higher-tier exposure assessment;
-How EPA will communicate Tier-1 exposure screening-level results;
-The higher-tiered information and models EPA will use to address human exposures, suggested by the results of the screening-level information/models;
-How EPA might use tiered exposure evaluations for specific exposure scenarios (e.g., occupational, consumer, residential, etc.);
-What kind of data and information EPA would accept (i.e. from stakeholders) to refine a Tier-1 screening exposure assessment.

Y			
Y			

17	ACC	3	Exposure	N/A
18	ACC	3	Exposure	N/A

TSCA Section 26(l) requires EPA to develop "policies, procedures and guidance that the Administrator determines are necessary to carry out the amendments" of amended TSCA. EPA indicates its intent to use tiered approaches in TSCA risk evaluations, but guidance is needed. EPA should develop new, more specific guidance on its plans to use tiered approaches to exposure assessment in TSCA risk evaluations. In doing so, EPA must move beyond mere "concepts" and reference lists to specific information, models, and tools. As stated earlier, EPA should indicate how PRA, uncertainty analyses, and the use of statistical tools would be integrated as a higher tier assessment. Specific and transparent guidance is needed to understand how the Agency will conduct its exposure assessments so that manufacturers can provide the most relevant information early on in the process to the Agency and so that stakeholders understand the process. As stated earlier, EPA should indicate how PRA, uncertainty analyses, and the use of statistical tools would be integrated as a higher tier assessment. Such guidance will also allow stakeholders to provide additional information to refine initial lower tier exposure estimates. Further program-specific guidance is also needed for those manufacturers that plan to conduct risk evaluations for EPA's consideration and must conform to EPA's approach to risk evaluations should they do so. Guidance on tiered approaches will help streamline the risk evaluation process under TSCA and enable EPA to meet TSCA's new mandates.

Canada's Chemical Management Plan (CMP), Australia's Inventory of Chemical Substances,23 and the EU's Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) program24 employ tiered approaches in their exposure assessment approaches for chemicals. EPA should review those approaches to ascertain their usefulness in new EPA guidance on tiered exposure assessments in TSCA risk evaluations.

Y			
Y			

19	ACC	3	Exposure	N/A
20	ACC	3	Exposure	N/A

According to EPA's problem formulations, EPA plans to further analyze occupational exposures in nine of the 10 chemicals risk evaluations. EPA must be more transparent about its coordination with OSHA regarding its plans to address occupational exposure issues in TSCA Section 6 risk evaluations. The methods, models, and databases that the Agency uses to conduct its occupational exposure assessments must be adequate to satisfy TSCA's Section 26 standards for best available science and weight of the scientific evidence. EPA should be more transparent about the OSHA and NIOSH databases that EPA plans to rely upon in these risk evaluations. Greater transparency will provide manufacturers notice about the type of information EPA may not have, but may need, to conduct a realistic occupational exposure assessment.
In eight of the problem formulation documents, EPA has identified OSHA's Chemical Exposure Health Data (CEHD) and NIOSH's Health Hazard Evaluation (HHE) program data as two major sources of occupational monitoring data that it will rely upon in the risk evaluations. However, EPA does not discuss what information in these databases it plans to rely upon; how representative the data are; what criteria EPA will use in deciding which data are or are not applicable for its exposure assessments; or how it plans to assess those data in the context of current OSHA regulations and industrial hygiene practices. EPA must provide greater detail about its use of the information in these OSHA and NIOSH databases to enable stakeholders to comment upon the data quality for the purposes for which EPA plans to rely upon the data, and to provide the Agency higher quality data where it exists.

Y			
Y			

20 cont	ACC	3	Exposure	N/A
21	ACC	3	Exposure	N/A

For instance, it is our understanding that the OSHA CEHD information does not include a description of the activities associated with the specific exposure measurements. Without this information, how will EPA be able to apply these results to the conditions of use identified for a chemical? Absent sufficient knowledge of activities associated with occupational exposure measurements, EPA might very well improperly assign exposure values to a certain condition of use/application. This could result in inappropriate conclusions about risk under specific conditions of use or risk management recommendations for protection of workers. It appears that this database reports non-detects (ND), but it does not specify the limit of detection (LOD). Without an understanding of the accuracy of the data, how will EPA use this data to inform estimates of exposure? In occupational settings, potentially hazardous exposures are eliminated or minimized by the use of training, industrial hygiene programs, engineering controls, closed systems, personal protective equipment (PPE), labeling, medical surveillance, etc. Over the past several decades, these engineering and industrial hygiene practices have continually improved. For example, as part of ACC's Responsible Care® Program, ACC member companies must implement ACC's Process Safety Code, which aims to supplement existing process safety requirements contained within the Responsible Care Management System® and RC14001® technical specifications. The Process Safety Code is intended to complement regulatory standards that, by necessity, focus on process safety at an individual facility. Another concern with the OSHA CEHD database is that much of the data were developed during inspections of facilities suspected of having high employee exposures. This suggests these data are not representative of occupational exposures from facilities that are in compliance with OSHA standards. EPA should address this fact in its quality review of the data/information underpinning its risk evaluations.

ACC understands that some ACC members have provided EPA with occupational monitoring information for use by the Agency in problem formulations for some of the initial 10 chemicals, but this information was apparently not reflected in the problem formulations issued on June 11, 2018. EPA should be clear in the draft risk evaluations how such submitted occupational monitoring information was used to prepare the problem formulations and considered in the risk evaluation.

Y			
Y			

22	ACC	3	Exposure	N/A
23	ACC	3	Exposure	N/A
24	ACC	3	Exposure	N/A

EPA indicates it plans to further analyze occupational exposures in the draft risk evaluations in nine of the 10 problem formulations. EPA has conducted very few worker exposure assessments on existing TSCA chemicals in the past and its Exposure Factors Handbook does not address occupational exposures.EPA has occupational exposure tools that are designed for specific purposes. For example, ChemSTEER was developed as a conservative screening tool used to estimate workplace exposures and environmental releases for new chemicals that are manufactured and used in industrial/commercial settings. However, broad guidance is not currently available for evaluating occupational exposures under TSCA, in particular with respect to the evaluation of existing chemicals. EPA should develop new guidance for evaluating occupational exposures under TSCA. To develop this guidance, EPA should certainly consider its own information, models, and tools on occupational exposure. EPA should also update some of its older tools and methods to evaluate worker exposure. EPA should update its 1997 Generic Scenarios for industry-specific workplace release and exposure estimation to make certain they reflect current industry practice. Many industrial practices in use today go beyond the legal regulatory requirements of OSHA. EPA should consider current industrial hygiene practices as part of the conditions of use of manufacturing. Additional Generic Scenarios may need to be developed to cover conditions of use for which Generic Scenarios do not currently exist.

It is also critical that EPA consider other information and tools available from OSHA, from the American Industrial Hygiene Association (AIHA), and from other jurisdictions to develop new occupational exposure guidance for TSCA purposes. EPA should consider the applicability of new models being used in Canada and the EU in their chemical regulatory programs. In considering information and tools from OSHA, AIHA, and other jurisdictions, EPA should also consider the adequacy and appropriateness of use of those tools in the TSCA context.

With respect to dermal exposures, the problem formulation documents identify several models for application to four of the 10 chemicals. EPA's existing dermal exposure assessment guidance is primarily geared toward neat compounds in soil or water, and it is not clear whether this guidance is sufficient to evaluate chemicals encountered in industrial-use scenarios.

Y			
Y			
Y			

25	ACC	3	Exposure	N/A
26	ACC	3	Exposure	N/A
27	ACC	3	Exposure	N/A
28	ACC	3	Exposure	N/A

For inhalation exposures, EPA has identified several models it plans to use in nine of the problem formulations. EPA guidance on potential inhalation exposures in occupational conditions of use under TSCA would be helpful.
Guidance on occupational exposure assessment under TSCA should address how the Agency will consider standard industrial hygiene practices as well as how that information will be incorporated into its exposure assessments and how ultimately that information will be integrated into the risk evaluation. EPA should address and identify the specific information the Agency will need to accomplish these steps; the level of detail needed to enable the Agency to reach a determination about the adequacy of design measures such as: closed systems; the use of engineering controls and labeling requirements (e.g., the use of gloves or other PPE); and other operating procedures and management practices currently in use to eliminate or adequately minimize exposures in occupational settings. EPA should describe how these considerations are incorporated into a tiered occupational exposure assessment.
EPA may need to gather information from industry regarding current occupational exposure protection practices. Industry may be able to facilitate access to that information. Manufacturers and organizations like AIHA may be able to help the Agency gather information about exposure data in occupational settings and industrial hygiene practices in various workplace situations. Ultimately, through such efforts, an EPA exposure factors handbook for occupational exposures could potentially be developed to address TSCA risk evaluation needs.
Consistent with application of a tiered approach to assessing exposure, EPA should articulate what kind of data will be acceptable to refine an initial lower tier occupational exposure assessment. For example, if a screening level estimate from ChemSTEER needs to be refined, a road map (as described above) would be a key element of guidance to develop the necessary information to conduct a higher tier assessment.

Y			
Y			
Y			
Y			

29	ACC	3	Exposure	N/A
30	ACC	3	Exposure	N/A
31	ACC	3	Exposure	N/A

EPA should be more transparent about specific exposure models, margins of exposure and occupational exposure limits that it intends to utilize during the risk evaluation process. This will allow stakeholders to provide the Agency the exposure information it needs and can lead to better understanding as to how EPA will make risk determinations.
ACC agrees with EPA's support for using tiered approaches generally, and in exposure modeling in particular. Under a tiered, iterative approach, screening-level tools, which are "protective by design," may be used initially. For substances that appear to present potential risks following a screening-level assessment, EPA should then proceed to use higher-tier tools. By beginning with screening-level assessments—which use more conservative assumptions and information than higher tier models—the Agency can optimize resource allocation by identifying exposure routes that present less risk early in the assessment process. When a Tier-1 screening assessment indicates low risk for a particular condition of use, the Agency should have a high degree of confidence that the potential risks are lower or perhaps nonexistent.
It is critical that EPA establish clear and consistent guidance that defines when Tier-1 model results will trigger more detailed and refined subsequent assessments. In the problem formulation documents, EPA frequently cites regulatory and non-regulatory occupational exposure limits, but it neither clarifies how it would apply these limits during an exposure assessment, nor specifies a process that will be followed should the Tier-1 model results exceed these limits or margins of exposure. In the event that EPA uses threshold triggers for Tier-2 models within EPA's risk assessment process, the Agency must provide guidance regarding how it selects these values and provide stakeholders an opportunity to comment.

Y
Y
Y

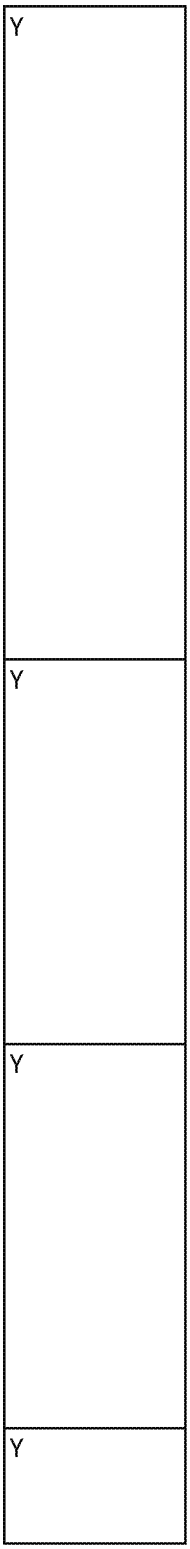
32	ACC	3	Exposure	N/A
33	ACC	3	Exposure	N/A
34	ACC	3	Exposure	N/A

Similarly, EPA should specify which exposure models—for all routes and populations—it intends to use during the risk evaluation process. In the problem formulations, EPA mentions several different models, but it does not provide rigorous guidance as to which tools will be used under which circumstances. Similarly, EPA does not identify specifically what it considers to be "higher tier models." Exposure models vary in terms of the purposes for which they are used, their input requirements, and assumptions. By providing a rationale for its model selection, the Agency will afford stakeholders an opportunity to provide appropriate data and contribute relevant information to EPA during its risk evaluations.
EPA also should be clear about the use of modeled vs. measured data in evaluating exposure. For example, if measured data are rejected in favor of modeled estimates, the rationale for such a decision needs to be clear.
EPA participates in the OECD's Working Party on Exposure Assessment (WPEA). In that capacity, EPA has been a global leader helping harmonize chemical use categories and developing standard exposure/emission scenario documents (ESDs) for occupational exposure assessments for chemical regulations. ACC expects that EPA will use these standard exposure scenarios in its occupational exposure assessments, but that is not clear from the problem formulation documents. EPA should clarify this point in its draft risk evaluations of these 10 chemicals and in any new guidance the Agency develops on exposure assessments under TSCA.

Y
Y
Y

35	ACC	3	Exposure	N/A
36	ACC	3	Exposure	N/A
37	ACC	3	Exposure	N/A
38	ACC	3	Exposure	N/A

In addition, EPA should develop additional standard exposure scenarios for both worker and consumer exposures under TSCA. Standard exposure scenarios would assure greater consistency in EPA exposure assessments; improve exposure model parameters; and help industry understand what specific information EPA needs in exposure assessments for TSCA risk evaluations. In short, standard exposure scenarios would improve efficiencies when conducting TSCA risk evaluations, which are critical given TSCA's statutory deadlines. EPA may want to consider stakeholder workshops to discuss ways in which standard exposure scenarios might be developed in the US. If so, EPA should also ensure that standard scenarios developed under REACH be discussed and considered at such workshops since many of these may be useful in TSCA as well.
EPA Should Explain What Additional Ecological Exposure Assessment Tools Are Available. The screening-level approaches described in the problem formulation documents are appropriate for this step (i.e., E-FAST), but EPA should identify acceptable tools/methods for higher-tier refinement when necessary. Screening-level exposure analysis may be suitable in cases where estimates do not exceed the Concentration of Concern (COC). EPA should explain how it would use higher-tier information, if provided.
EPA has indicated that environmental exposure data may be available for some of these 10 chemicals in the EPA Discharge Monitoring Report tool, EPA's STOrage and RETreival (STORET) system, USGS National Water Quality Assessment (NAWQA) program, and other sources. Some of these data sources may not be current and therefore may not represent the best available information. EPA should clarify exactly how it would use such data to establish a national, regional, or local environmental exposure estimate.
EPA should also clarify how it will quantify and assess (or exclude) naturally-occurring sources of chemicals for assessment during exposure estimation.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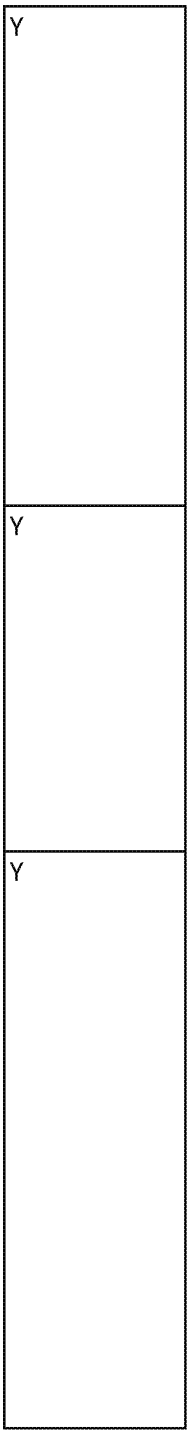
39	ACC	3	Exposure	N/A
40	ACC	3	Exposure	N/A
41	ACC	3	Exposure	N/A

EPA's Consumer Exposure Model (CEM) is mentioned as the preferred tool for estimating consumer exposures in several of the first 10 chemicals' risk evaluations. This model is publicly available. However, another model mentioned by EPA is the Multi-Chamber Concentration and Exposure Model (MCCEM). This model is available on EPA's exposure tools website, but in a version (Windows 95 operating environment) that will not run on currently available platforms. EPA should ensure that all the models it uses in its assessments are publicly available in a form that is accessible to the general public, complete with explanations on how to use the model and how the exposure endpoints are estimated.
The problem formulations for most of the 10 chemicals indicate that the chemical is found in either formulated products used by consumers or in articles with which consumers could come into contact. It is not clear how EPA will assess consumer exposures to these products. The exposure assessments must be able to estimate the consumer exposures from these chemicals based on whether they are found in formulated products or articles.
For chemicals that are primarily in articles, the approach and rationale for estimating consumer exposures should be described in detail because exposure assessments from articles are a new area of assessment. Industry and other stakeholders may not be familiar with the rationale and approaches used to estimate exposures from articles. The scientific basis for determining exposures from chemicals in articles must be established for the Agency to meet the statutory standard that requires TSCA risk assessments to quantify the likely (i.e., having a high probability of being true) duration, intensity, frequency, and number of exposures under the conditions of use. EPA should clearly identify the criteria for and scope of the tools chosen to be used in each circumstance.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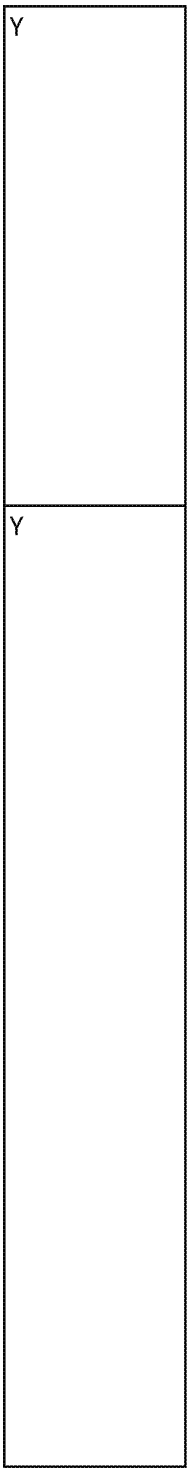
Y

42	ACC	3	Exposure	N/A
43	ACC	3	Exposure	N/A

For exposure assessments, EPA may need to make decisions about which products to focus on in the assessments among the various potential products in which the chemical may be found. To conduct the consumer exposure assessment, the assessor may need to focus on representative products in some of these use categories. The product types chosen to be used in the exposure models, the exposure routes, most relevant exposure scenarios, exposure endpoints, and rationale for the choices must be described. The greater the clarity and transparency of these explanations, the greater the likelihood the final assessment will be understood.

EPA states in several of the problem formulations that TRI data will be used as a source of information on releases to the environment. TRI data may have a role to play as an element in chemical prioritization, but these data also have limitations. EPA states on the TRI website: [The Toxics Release Inventory (TRI) provides data about environmental releases of toxic chemicals from industrial facilities throughout the United States, measured in pounds. The quantity of releases, however, does not indicate the level of health risk posed by the chemicals. Although TRI data can't tell you whether or to what extent you've been exposed to these chemicals, they can be used as a starting point in evaluating potential risks to human health and the environment.] EPA readily acknowledges in its TRI National Analysis 2016: Releases of Chemicals that "[h]uman health risk resulting from exposure to toxic chemicals are determined by many factors..." These factors include environmental fate, individual exposures, chemical properties, and concentration, none of which are furnished through the TRI. For a chemical to present a risk, there must be a sufficient pathway and exposure, factors that TRI does not address. EPA should acknowledge and explain the limited value of TRI data in risk evaluation.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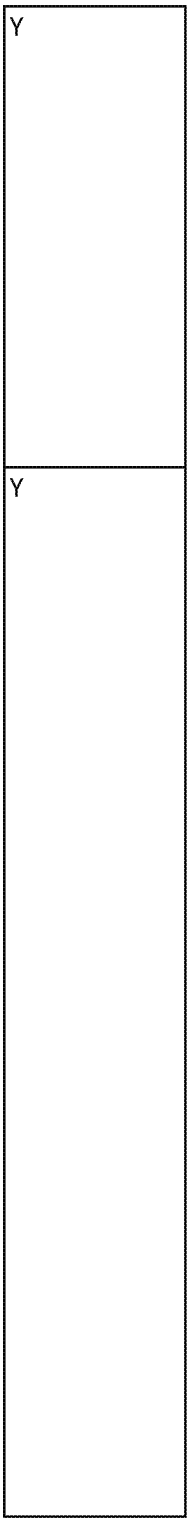
44	ACC	3	Exposure	N/A
45	ACC	3	Human Health	N/A

Biomonitoring information is identified in several of the problem formulations as a type of data/information source for TSCA risk evaluations, but there is limited discussion of how or where it would be used. EPA should address in guidance the specific biomonitoring information it would rely upon in TSCA risk evaluations and how it would be used. Canada uses "biomonitoring equivalents" in its risk assessments under the Canadian Management Plan (CMP). EPA should examine how those values, as well as Canada's assessments that are based upon them, might be used in the TSCA exposure assessments.
It is important that a multidisciplinary review process, which integrates hazard information and data from in vitro and in vivo studies across different biological levels of organization for a given exposure scenario, be established for hazard evaluation, data review, and decision making contexts. Typically, this should be a transparent and structured analysis using the Bradford Hill causal considerations and, in particular, biological plausibility and empirical support (dose response, temporal concordance and consistency). The hazard information must be relevant to the specific exposure scenario and the integration of data should be applied initially for each data stream (epidemiology, in vivo, mechanistic) across similar types of study endpoints. The lines of evidence (human epidemiology, in vivo toxicity and mechanistic) must then be integrated using a transparent and objective approach. Through such an integrated assessment, evaluators use the entire body of studies and the full weight of the scientific evidence. This approach avoids the pitfalls of selecting the lowest statistically significant finding of a response in a given study (as a default) without adequately framing the risk hypotheses and integrating data from different sources. EPA states in the general response to comments on the initial 10 scope documents that it anticipates using data from alternative test methods for the risk evaluations. This is consistent with the mandate under TSCA Section 4(h) to "reduce and replace, to the extent practicable, scientifically justified, and consistent with the policies of this title, the use of vertebrate animals in the testing of chemical substances or mixtures..."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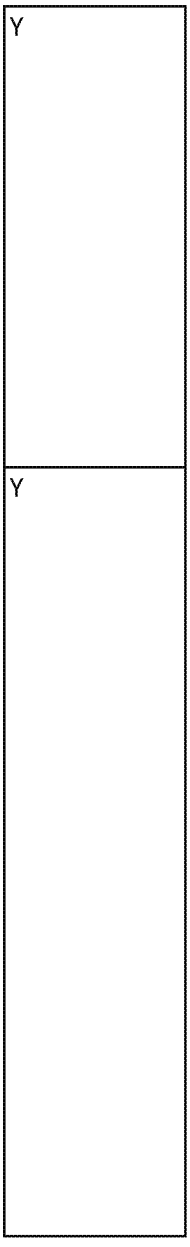
Y

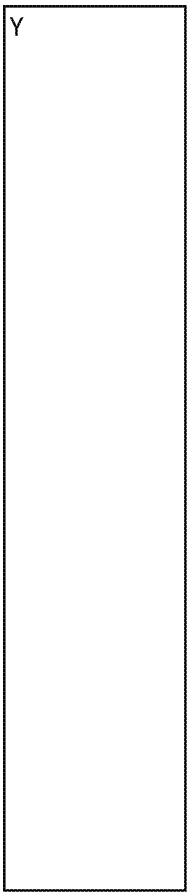
46	ACC	3	Human Health	N/A
47	ACC	3	Human Health	N/A

ACC supports EPA's continued efforts to identify, develop, and integrate new approach methodologies (NAMs) for regulatory decision-making according to the EPA OPPT Strategic Plan to Promote the Development and Implementation of Alternative Test Methods. It is important that sufficient scientific confidence in each NAM be established for its intended application before use as a key piece of evidence in a hazard evaluation and limitations be acknowledged. It is equally important that exposure information, at a fit-for-purpose level of resolution, is available to place these data into a risk context.
EPA acknowledges that it must further analyze the MOA for cancer risk in the problem formulations. ACC supports that analysis. The AOP framework is a tool to systematically organize available data and knowledge that describes scientifically plausible and causal relationships across multiple levels of biological organization between a molecular initiating event (MIE) and subsequent key events (KEs), culminating in an adverse outcome (AO) potentially relevant to risk assessment. EPA researchers have been instrumental in developing AOPs and tools to facilitate the further development, review, and use of AOPs in scientific and regulatory endeavors. Tools such as the AOP wiki can be mined for additional data and organizational principles as well as domains of applicability for various identified MOAs associated with chemicals. Thus, whether evidence generally aligns or does not align with any proposed or known MOAs and/or AOPs should be a necessary consideration in integrating evidence to reach conclusions.


Y
Y

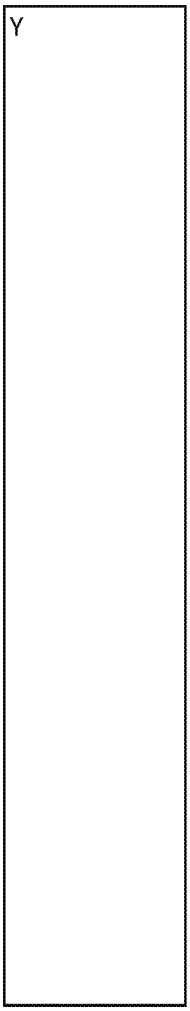
48	ACC	3	Human Health	N/A

The Agency's focus on dose-response data and models reflects the fact that toxicology has evolved over the past 35 years from a largely observational field of study to a discipline that applies advanced scientific techniques and knowledge to investigate how chemicals interact with biological systems at the molecular, cellular, organ, and organism levels to understand the biological basis for the induction of toxicity. As a consequence of rapid advances in scientific understanding and the application of this knowledge to regulatory science policy and risk assessments, risk assessors can now evaluate biological events leading to toxicity and consider how, in a dose-response manner, these events relate to potential risks to human health. Despite the significant progress, movement away from default assumptions has been slow to occur, particularly in certain EPA programs. Failure to recognize and act on advances in scientific knowledge and the best available, most relevant scientific data and dose response models wastes significant research and development investments. It is also contrary to the TSCA Section 26 requirement that EPA rely upon best available science in science-based Section 6 decisions.


Y

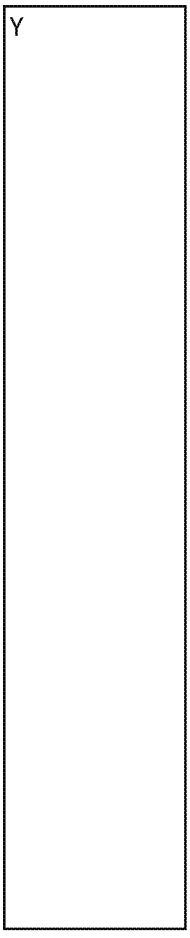
49	ACC	3	Human Health	N/A

In its 2005 Cancer Guidelines, EPA is clear that when risk assessments are performed using only one set of procedures, it may be difficult for risk managers to determine how much health protection is built into a particular hazard determination or risk characterization. EPA's Cancer Guidelines state:[When there are alternative procedures having significant biological support, the Agency encourages assessments to be performed using these alternative procedures, if feasible, in order to shed light on the uncertainties in the assessment, recognizing that the Agencymay decide to give greater weight to one set of procedures than another in a specific assessment or management decision.] In addition, the Agency says: [If critical analysis of agent-specific information is consistent with one or more biologically based models as well as with the default option, the alternative models and the default option are both carried through the assessment and characterized for the risk manager. In this case, the default model not only fits the data, but also serves as a benchmark for comparison with other analyses. This case also highlights the importance of extensive experimentation to support a conclusion about mode of action, including addressing the issue of whether alternative modes of action are also plausible.] These statements are related to comment 50.


Y

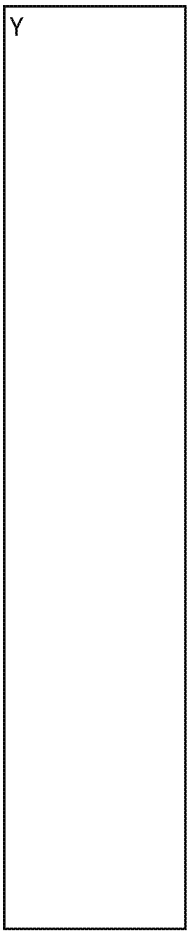
50	ACC	3	Human Health	N/A

EPA's Office of Pesticide Programs (OPP) has adopted the World Health Organization (WHO)/International Programme on Chemical Safety (IPCS) MOA framework for organizing, evaluating, and integrating hazard and dose response information. The same approach should be adopted for TSCA assessments. The MOA framework can be used to illustrate the key events in a known toxicity pathway to address whether a reported statistically-significant response is consistent with what is expected based upon knowledge of the biological responses comprising the pathway. It should be noted that even if early biological responses/perturbations are detected, these observations are not necessarily adverse or precursors to adverse effects in living organisms because of adaptive or homeostatic mechanisms. To reliably predict toxicity, key events need to be causally linked to adversity with a clear understanding of dose response/temporal key event relationships. EPA should adopt and use the standard MOA templates for both cancer and non-cancer endpoints, such as the dose/temporal concordance and species concordance templates. These templates have been incorporated by the European Chemicals Agency (ECHA) in implementing Europe's REACH program.


Y

51	ACC	3	Human Health	N/A

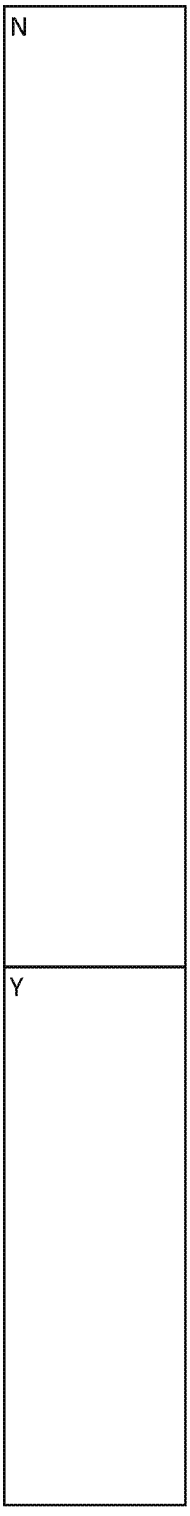
Because the scientific justification for assessing human relevance and selecting dose-response extrapolation methods for quantifying risks at environmentally relevant levels of exposure is highly dependent upon the determination of the likely operative MOA, the Agency should implement a uniform, systematic and explicit approach for evaluating a chemical dataset, using hypothesized MOAs and the evolved Bradford Hill causal considerations, to integrate evidence and derive weight of the evidence (WOE) confidence scores for potentially relevant MOAs. This approach enables a side-by-side comparison of numerical WOE confidence scores for different hypothesized MOAs, including the default linear-no-threshold model, which permits better identification of the likely best MOA to use. The side-by-side quantitative MOA WOE confidence scoring method enhances transparency and improves communication amongst risk managers and the public. Furthermore, the best available science approach provides a transparent, scientifically sound justification for using the most likely operative MOA as the basis for selecting the most appropriate extrapolation method that corresponds to that MOA to then calculate potential risks to humans for environmentally relevant exposures.


Y

52	ACC	3	Human Health	N/A
53	ACC	3	Human Health	N/A

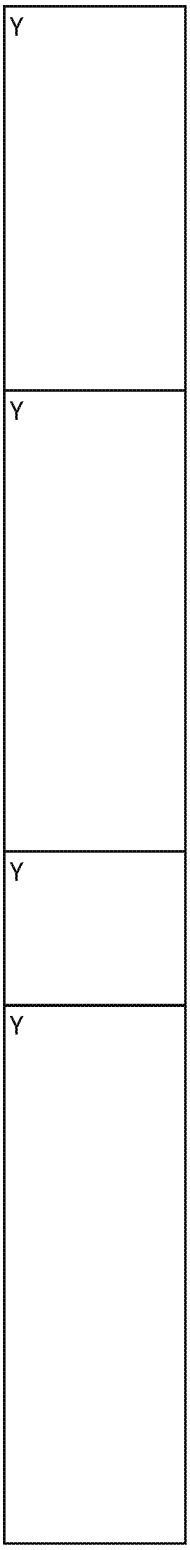
To illustrate this method, a case example has been developed based on data of rodent liver tumors induced by carbon tetrachloride (Attachment B-attached in the ACC coments on Problem Forumulation 46 August 2018). This case example used data and lines of evidence from previously published review articles, and relied on those authors' evaluations of the quality of the empirical evidence. Two hypothesized MOAs were evaluated: 1) induction of rodent liver tumors via a mutagenic MOA; and 2) induction of rodent liver tumors via a cytotoxicity MOA. The quantitative MOA WOE confidence scoring results of this case example indicate: (1) it is highly unlikely that carbon tetrachloride induces rodent liver tumors via a mutagenic MOA and (2) Cytotoxicity and sustained regenerative cellular proliferation is the like operative MOA for induction of liver timors in rodents by carbon tetrachloride; there are significant mechanistic data to support thos non-linear, non-mutagenic MOA. Based on the comparison of quantitative MOA WOE confidence scores, there is strong scientific support for using a threshold extrapolation approach for evaluating the cancer risks of carbon tetrachloride. (In contrast, scientific justification is lacking to support a linear, no threshold extrapolation method for evaluating its cancer risks.)

Finally, another challenge in extrapolating animal data to human data involves having an understanding of the relative toxicokinetics. Significant strides have been made using physiologically based pharmacokinetic (PBPK) data and models in risk assessment to improve the accuracy of deriving dosimetry considerations. However, it is important to recognize that some animal studies using conventional maximum tolerated doses (MTDs) are flawed and cannot be used to extrapolate to human doses because they exceed the kinetically-derived maximum dose (KMD). In a number of cases, substances show dose-dependent transitions in their mechanisms of toxicity. This circumstance needs to be evaluated appropriately.


N
Y

54	ACC	3	Eco Health	N/A
55	ACC	3	Eco Health	N/A
56	ACC	3	Eco Health	N/A
57	ACC	3	General	N/A

EPA has used a simple approach to calculate the acute and chronic COCs, i.e., dividing the lowest study value by an assessment factor. Conservative, screening-level approaches, such as those utilized in the EPA's New Chemicals Program, can be appropriate to provide context at the problem formulation stage. However, in future scoping documents EPA should clarify the circumstances under which further, higher-tier evaluation would be triggered, if necessary (e.g. species sensitivity distribution, etc.).
EPA should identify more sophisticated higher-tier approaches it may use for determining a hazard threshold, especially for data rich chemicals. Toxicity information, and when available, knowledge of mechanisms, are integrated with exposure-response models for risk-based environmental safety decision making. Within an environmental context, the assessment of safety does not end at the organism, but includes extrapolation to populations, communities, and ecosystems. For ecological risk assessment, the possibility of obtaining site-specific population data is a critical option for higher-tier assessment.
EPA should also consider the unique physico-chemical properties that can impact substances' pharmacokinetics and toxicity profiles, as well as their environmental fate and distribution.
Conclusion: ACC commends EPA on its efforts to gather the best available information for the problem formulation documents for the initial 10 chemicals undergoing risk evaluation under amended TSCA. EPA has demonstrated some screening-level assessment techniques that allow EPA to focus on the conditions of use that pose the greatest potential for risk. However, in situations where EPA may need to perform higher tier assessments for the risk evaluation, more guidance and information is needed on the types of data and techniques that EPA will utilize. This will enable industry to better understand how to provide EPA with the information it needs to perform high quality risk evaluations.


Y
Y
Y
Y

58	APHA	1	Exposure	N/A
59	APHA	1	Exposure	N/A
60	APHA	1	Exposure	N/A

TSCA is EPA's primary source of authority for evaluating and managing the health and environmental risks presented by approximately 85,000 industrial chemicals. Unfortunately, the problem formulation documents indicate that the agency intends to conduct risk evaluations that are incomplete and likely to underestimate risk. Specifically, the agency plans to ignore numerous exposures to these chemicals. By considering only some exposures and not others, EPA likely will conclude that the total level of exposure to a chemical is lower than it truly is. The agency then may determine incorrectly that this lower level of exposure does not present an unreasonable risk of injury to health or the environment, even when the true level of exposure does present such a risk. The decision to ignore chemical exposures is unlawful and lacks scientific credibility. EPA should include all exposures to these chemicals in its risk evaluations.

EPA's problem formulation documents indicate several ways in which the agency intends to ignore exposures to the chemicals. First, TSCA requires EPA to "conduct risk evaluations…to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment…under the conditions of use." TSCA § 6(b)(4)(A) (emphasis added). In general, "the conditions of use" of a chemical include the manufacture, distribution in commerce, processing, use, and disposal of the chemical. EPA has decided to ignore conditions of use and resulting exposures, either by declaring that certain activities are not conditions of use or by acknowledging that the activities are conditions of use but nonetheless declaring that they will not be included in the risk evaluation. These actions by the agency lack both legal and factual support.

Second, EPA has decided to exclude entire exposure pathways, such as inhalation of a chemical in ambient air or ingestion of a chemical in drinking water, from the risk evaluations. These exclusions rely on a flawed analysis of TSCA and other environmental statutes. Furthermore, EPA admits the exclusions will disregard important risks of injury to health.

Y
Y
Y

61	APHA	1	Exposure	N/A
62	APHA	1	Exposure	N/A
63	APHA	1	Exposure	N/A
64	APHA	1	Exposure	N/A
65	APHA	1	Exposure	N/A

The exclusion of certain activities from the risk evaluations is unlawful. As noted above, TSCA requires EPA to evaluate the risks presented by "a chemical substance" under "the conditions of use." The language of the statute clearly directs the agency to evaluate the risk presented by a chemical substance in total and does not provide for picking and choosing among conditions of use when conducting a risk evaluation. Even if EPA did possess the authority to include only some conditions of use and not others, however, the agency still has failed to support its exclusions with information provided in the problem formulation documents.
In many cases, it appears that EPA has obtained information via unverified communications with companies that once engaged and still may be engaged in activities that constitute conditions of use. These include manufacturers, processors, distributors, commercial users, and companies involved in disposal of one or more of the chemicals. It does not appear that EPA has taken meaningful steps to verify information provided by companies or their representatives. This is inappropriate due to the obvious conflicts of interest with respect to risk evaluations for chemicals that once were or still are important to their businesses.
For example, EPA has concluded that "domestic manufacture of HBCD has ceased" based primarily on assurances provided by two recent manufacturers of the flame retardant. The agency does not indicate how it verified these assurances or how it will ensure that the purported cessation will continue in the future.
EPA relies on information from entities even after concluding that the information is not credible.
Even if the information provided by a company is accurate, the company remains free to resume any activity at any point in the future absent a regulation stating otherwise. Such an activity therefore remains a "reasonably foreseeable" condition of use under the statute. Furthermore, accurate information that may be provided by one company or subset of companies cannot be assumed to represent the activities of all current or future firms within an industry. Yet EPA makes this assumption.

Y
Y
N
Y
Y

66	APHA	1	Exposure	N/A
67	APHA	1	Exposure	N/A
68	APHA	1	Exposure, RegNex	N/A
69	APHA	1	Exposure, RegNex	N/A
70	APHA	1	Exposure	N/A

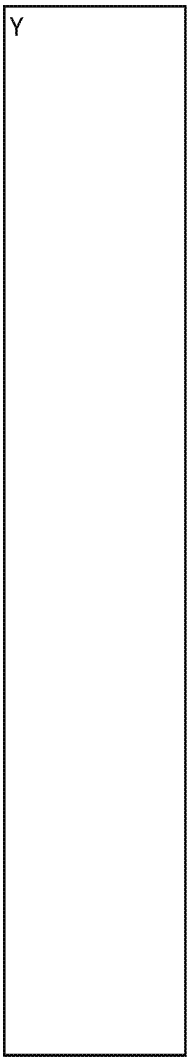
At a minimum, if EPA is told that manufacture, import, and processing of a chemical has ceased, the agency should demand legally binding certification of such cessation from every previous manufacturer, importer, and processor of the chemical. Furthermore, the agency should promulgate a significant new use rule under TSCA § 5(a) so that, if and when manufacture, import, or processing of the chemical does occur in the future, the activity must be reported to EPA.
In addition to ignoring conditions of use, EPA intends to disregard entire pathways of exposure to chemicals. By disregarding these pathways, EPA will narrow the scopes of the risk evaluations further. In addition, for every chemical except pigment violet 29, EPA argues it can ignore exposures resulting from disposal. By excluding pathways, the agency will ignore potential exposure to more than 68 million pounds of industrial chemicals released each year. EPA's rationale for excluding pathways disregards TSCA and, by the agency's own admission, ignores unreasonable risks of injury to health.
According to the agency, exposure pathways will be excluded when they fall under "other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist[.]" There are key differences between the requirements imposed by "other environmental statutes" and the requirements imposed by TSCA.
EPA is required to evaluate the risk presented by chemicals under TSCA. This includes any risks to vulnerable populations. The agency cannot escape this requirement by ducking behind unrelated statutes that impose separate requirements to protect public health.
EPA admits that excluding exposure pathways will neglect unreasonable risks of injury to health presented by the chemicals.

Y
Y
Y
Y
Y

71	APHA	1	PESS	N/A

TSCA requires EPA to determine whether a chemical presents an unreasonable risk of injury to the general population and/or to "potentially exposed or susceptible subpopulations." §6(b)(4)(A). A potentially exposed or susceptible subpopulation is any "group of individualswithin the general population…who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population…such as infants, children, pregnant women, workers, or the elderly." § 3(12). It is well understood, for example, that pregnant women, children, and infants are uniquely susceptible to chemical exposures. TSCA imposes a duty on
EPA to ensure that vulnerable subpopulations are protected from chemical risks, and it is imperative that the agency conduct risk evaluations, make risk determinations, and promulgate risk management regulations in accordance with this duty.

In particular, TSCA provides new tools to protect workers from occupational exposures to a wide variety of chemicals encountered while on the job. Workers face significant risk of harm from chemical exposures but they are not adequately protected by regulations of the Occupational Safety and Health Administration. OSHA has adopted comprehensive health standards on just a few dozen chemicals since the agency was established in 1971, and most of these standards were issued before 1990.25 Furthermore, tens of millions of workers are not covered by the Occupational Safety and Health Act. EPA's duty to protect workers and other
vulnerable subpopulations under TSCA fills in gaps in the law that have allowed workers to go unprotected from chemical hazards.


Y

72	NTTC	1	Exposure, General	N/A
73	NTTC	1	PESS, General, Exposure	N/A

Beyond the clear primary issue to Tribes of the absence of tribally-specific risk scenarios in the problem formulation, NTTC further takes issue with the following critical points that relate to the problem formulations in general and prevent the performance of a valid health assessment for tribes and other Americans as intended by Congress:
-Omission of legacy use, particularly the use and disposal of products that are still in active service life. For example, it is unclear why the widespread use and disposal of millions of computers and other electronics known to contain HBCD is not considered in the problem formulation.
-Omission of conditions of use considered to be under the purview of other Federal Environmental Statutes that focus primarily on priority pollutants. TSCA was amended specifically because Congress found that these same existing environmental laws did not adequately protect the American people.
-Omission of products knowingly or reasonably foreseen to incorporate HBCD and the complete omission of recycled products due to a perceived 'lack of intention' in fitting the Administrator's narrowly defined Conditions of Use. For example, the use and disposal of picture frames, food trays, coolers, and other products knowingly made with recycled EPS of high HBCD content is not considered.
The decisions taken by EPA on these points were spurious and each are clearly inconsistent with the science and purpose of risk assessment and TSCA itself.

As currently practiced, the proposed conceptual models of the first ten problem formulations issued
May 2018 do not meet the standard of relevance and representation for Tribal peoples, and therefore the model implementation process is essentially moot, and the applicability of the model to the 6.1 million people that Tribes represent is irrelevant.

74	NTTC	1	General, Exposure	N/A

We use the commonly accepted definitions of key terminology in risk assessment science. The following excerpts are drawn from the International Programme on Chemical Safety (IPCS) glossary (2004)3 and the Principles of Characterizing and Applying Human Exposure Models (2005)4 as published by the World Health Organization. Exposure assessment is "The process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent, along with the number and characteristics of the population exposed. Ideally, it describes the sources, pathways, routes, and the uncertainties in the assessment" (IPCS, 2004). Exposure assessment is used in epidemiological studies to relate exposure concentrations to adverse health outcomes. Exposure assessment is also an integral component of risk assessment, the process that provides scientific information for risk management. Exposure assessment is based on exposure scenarios, which are defined as "A combination of facts, assumptions, and inferences that define a discrete situation where potential exposures may occur. These may include the source, the exposed population, the time frame of exposure, microenvironment(s), and activities. Scenarios are often created to aid exposure assessors in estimating exposure" (IPCS, 2004). An exposure model is a computational framework designed to reflect real-world human exposure scenarios and processes. A conceptual model is often illustrated by a block diagram, and it defines the physical, chemical and behavioural information and exposure
algorithms by which the model mimics a realistic exposure scenario. … The implementation of an exposure model should reflect the underlying conceptual model. Whenever the exposures of different subpopulations are expected to be different from each other, the exposure assessment probably needs to treat these subpopulations separately.

75	NTTC	1	General, Exposure	N/A

Model evaluation can be seen as a three-step process:
-1.The conceptual model must be validated. ...The (causal) relationships between the model input events and the output events must be real, and the nature, or shape, of these relationships must be known — at least approximately.
-2.The model implementation must follow the conceptual model. The definitions of input and output variables must effectively describe the events of the conceptual model, and the algorithms and equations must sufficiently follow the true (causal) relationships of these events.
-3. Assessing the applicability of the model to a set of specific problems is possibly the most difficult step. This includes evaluating how well the input values really describe the target system. Usually the input values have been measured and contain random or systematic measurement errors. The measured input data range is a combination of data uncertainty and true inherent variability, and in some new applications it is essential to be able to differentiate between the two (e.g. when one or the other dominates the
distribution). Sometimes other models, questionnaire data or expert opinions are used in place of measurements to assign values to input variables Each of these inputs may or may not accurately describe the characteristics of the target system. Thus, even when the model is conceptually valid and carefully implemented, the model outputs may not agree with the system outputs.

76	NTTC	1	General, Exposure, PESS	N/A

In several of the following sections, the NTTC provides wide-ranging explanation of the vast extent of activities within tribal lifeways, aspects of "the system" (as referenced above) that needs to be modeled in the risk assessment process. In section 7 NTTC provides a graphic image of tribal lifeways, to provide a visual sense of the realm of all natural resources within tribal lifeways, and multitude of exposure scenarios and exposure pathways by which tribal populations are put at greater risk because their tribal lifeways have not been contained with TSCA risk assessment and risk evaluation processes. Also, in section 7, NTTC proposes the draft Possible Tribal Exposures Conceptual Model which received preliminary review and informal comment in an NTTC meeting with EPA OPPT earlier this year. Though in draft form, NTTC emphasizes that by using this conceptual model when evaluating unreasonable risk of injury to health (or their environment) to a potentially exposed and susceptible subpopulations, EPA will thereby protect both tribal populations and other subpopulations.

77	NTTC	1	General, Exposure, PESS	N/A

In terms of subpopulations, consider how Barzyk (2010) discussed community-based risk assessment: “One of the primary differences between communities is in their patterns of exposure. … Tools that isolate exposure routes and pathways for a given community and then incorporate toxicity information will lead to a better characterization of risk”. This is key when considering potentially exposed and susceptible subpopulations, such as tribal groups whose patterns of exposure can be considered to be the “community” of an eco-region, e.g., the Pacific Northwest could encompass tribes and their lifeways from northern California, northerly along the Pacific coast into British Columbia, Canada and as far as the Prince William Sound in southcentral Alaska, U.S.

-1. As currently practiced, the proposed conceptual models of the first ten problem formulations issued May 2018 do not meet the standard of relevance and representation for Tribal peoples, and therefore the model implementation process is essentially moot, and the applicability of the model to the 6.1 million people that Tribes represent is irrelevant.

-2. Risk assessment of Tribal peoples for TSCA contaminants found in environmental media is relevant because Tribes are in contact with soil, sediment, and water as much or more than other population groups.

-3. But the proposed problem formulations, and the risk assessments are not representative because they do not reflect nor model Tribal lifestyles. An entire population of people (6.1million strong) are not represented in any USEPA risk assessment work to date.

78	NTTC	1	General, Exposure, PESS	N/A
79	NTTC	1	General, PESS	N/A

For millennia, tribal cultures were completely synonymous with and inseparable from the land and its resources. Tribes (used throughout this document) includes tribal people, resources, and other interests; interests (as sovereigns, seeking to govern/regulate tribal resources and as proprietors, i.e., holders of rights to land, water, fish, etc.) and the interests of individual Native people (whether they are tribal citizens or not; whether they live on a reservation or not); it is important to encompass tribal members who do not reside on tribal land, usual and accustomed areas, as well as treaty-protected resources; tribal lands as used in this report includes reservations, ceded lands, Usual and Accustomed areas (U&A) as well as communities inclusive of the Alaska Native Villages
and Islanders and those without land bases. Continuing today, many tribes, tribal people and their clans are identified in their Native languages and in English translations as the name of singular or multiple seasonal locations or specific animals or insects, e.g. Water's Edge Clan (Navajo), People of the Herring Rock (Tlíngit), Where the Water Cuts Through (Po-wo-ge-oweenge), Red Willow Place (Tua-Tah), People of the standing of projecting rock or stone (Seneca), The Place where the locusts were taken out (Cayuga), The River with the two logs across it (Chickaloon).

Current Federal Indian Policy recognizes Tribal Sovereignty, Federal Trust Responsibility, and Government to Government Relationship, yet tribes today suffer health disparities, experience exposure pathways through tribal lifeways. Treaties are legally binding contracts between sovereign nations that establish those nations' political and property relations. Article VI of the U.S. Constitution holds that treaties "are the supreme law of the land." In return for taking vast Indian holdings and resources (i.e. land), the U.S. promised: Reservation Lands, Continued Sovereignty, Protection, Health Care, Education, Religious Freedom, Some Monies. Through the treaties they negotiated, tribes retained rights of self-government and jurisdiction. [exceprt from the 1855 Treaty with Yakama] Tribal sovereignty means that tribes are independent nations with the right to govern themselves by: Forming their own government, adjudicate legal cases within its boundaries, levy taxes within their borders, establish its membership, and retain government-to-government relationship with the U.S.

80	NTTC	1	General, PESS	N/A

The Federal Government has a trust responsibility to protect tribal lands, assets, resources, and treaty rights, and uphold the promises made when treaties were made. With these recognized responsibilities and rights, Tribes have a unique legal status with the U.S. government. They are neither foreign nations, nor states. Tribes are distinct political communities defined in law as “domestic dependent nations.” In the 1831 Cherokee Nation v. Georgia decision, the Supreme Court described the obligation of the U.S. to tribes as that of a guardian to his wards. Subsequent decisions have made it clear that the agencies of the federal government are to be held to the most stringent “fiduciary” (trust) standards. “Trust lands” describe lands held in trust by the U.S. for the benefit of a tribe or individual tribal member which cannot be alienated or confiscated through eminent domain. Additional case law since that 1831 Supreme Court decision confirms federal trust responsibility and protection tribal culture, identity, and ways of life. "Moral obligation of the highest responsibility and trust"-Seminole Tribs v. U.S. (1942). The United States is the trustee of Indian reserved rights, including fishing rights. -See, e.g., Joint Board of Control v. United States, 862 F.2d 195 (1988), 198 (9th Cir. 1988); Muckleshoot Indian Tribe v. Hall, 698 F. Supp. 1504, 1510-1511 (W.D. Wash. 1988). The obligation of the United States as trustee of Indian resources and rights extends to all agencies and departments of the Executive Branch. -See Pyramid Lake Paiute Tribe v. Department of the Navy, 898 F.2d 1410, 1420 (9th Cir. 1990), Covelo Indian Community v. FERC, 895 F.2d 581, 586 (9th Cir. 1990). The right to resort to the fishing places in controversy was a part of larger rights possessed by the Indians, upon the existence of which there was not a shadow of impediment, and which were not much less necessary to the existence of the Indians than the atmosphere they breathed.”)U.S. v. Winans, 198 US 371 (1905). “...the Indians reiterated...that they wished to reserve the privilege of using the land for gathering, hunting, and fishing activities. They said that they could not live, deprived of these means of sustenance.Lac Court Oreilles Band of Chippewa Indians v. Leter P. Voigt, Seventh Circuit Court (1983).

81	NTTC	1	General, PESS	N/A
82	NTTC	1	General, PESS, Exposure	N/A

Tribal nations, their governments, and their enrolled tribal members and tribal descendants are present in the United States and continue their ancestral tribal lifeways. There are 573 federally recognized tribes: 229 in Alaska, 110 in California and 234 in 33 other states. There are 61 state recognized tribes in 12 states. As of 2017, the U.S. Census Bureau's annual estimate of the Native American and Alaska Native population was 6.1 million which is 1.7% of the total U.S. population. Further, the Bureau projects that by 2050 the Native American and Alaska Native population will be 8.6 million, 2% of the total U.S. populations. The tribal nations with the largest populations include: Cherokee, Navajo, Choctaw, Chippewa, Sioux, Apache, Blackfeet, and Pueblo. The tribal lands—both trust lands and non-trust and non-reservation lands—accumulate to a collective geographical area today of 56 million acres which is equivalent to the size of Idaho state. Unfortunately, tribal people are afflicted by some of the least desirable statistics in the U.S.: the highest rates of suicide of any racial or ethnic group including white; highest rates of violence against women at more than double the rates of women of other races; overrepresentation in U.S. prisons and jails; historical and generational trauma from loss of people, lands and culture; posttraumatic stress disorder; more likely to have poorer overall physical and mental health and unmet medical and psychological needs; overrepresentation in the U.S. foster care system; and predisposition to heart disease, diabetes, and substance addiction. Many of these physical and mental health disparities are related to the historic and generational traumas, related to poverty induced by loss of people, lands, and language, related to the unmet obligations of the U.S. Government. These health disparities are exacerbated by environmental contaminants and pollutants in and around tribal resources. There is a legacy of toxic pollution on tribal lands and resources: "More than a century of hard rock mining has left a legacy of >160,000 abandoned mines in the Western USA that are home to the majority of Native American lands. ...Similar articles could be written focusing on impacts to tribal lands from coal strip mining, from the legacy of military bases, and from oil and gas development." Ineffective policies and the lack of infrastructure lead to environmental contamination through permitted exemptions to waste disposal allowing unlined landfills that accept household hazardous waste and unfiltered emissions from on-the-ground or other open burning. These exemptions also allow waste managers non-collection and non-treatment of landfill leachate. Additionally, tribal lands are commonly used for illegal waste dumping due to the significant void of law enforcement presence.

Despite attempts to disconnect tribes from traditional resources and tribal lifeways, tribal populations maintain a close relationship to the environment. The chemical exposures experienced by tribal people are not extremes of a general population range but consist of many discrete activities with legal protections. NTTC recognizes that prior to the Lautenberg Act, the burden of proof of toxicity was on the U.S.consumer. This is not adequate for the tribal community, especially considering the high-level consumption by tribal members of wild and natural resources as well as the U.S. government's trust responsibility and inability to provide safe water and sewer, and solid waste disposal on many Indian reservations and in many Alaska Native villages.

83	NTTC	1	General, PESS, Exposure	N/A
84	NTTC	1	General, PESS, Exposure	N/A
85	NTTC	1	General, PESS, Exposure	N/A

The below Graphic illustrates the unique exposures that Tribes face and that should be considered in any risk assessment procedure. The conceptual model that follows is intended for use in formulating the scope of any EPA chemical risk assessment. *See Conceptual Model Figures.* [Part 7, pages 10-11, presents a Conceptual Model of Tribal Exposures including a graphic reproduction and a flowchart]

NTTC supports EPA's comments on the September 30, 2015 technical call (U.S. EPA, 2015b) that EPA will evaluate additive exposures, such as oral exposures including fish consumption, drinking water consumption, potential for dust consumption and mouthing in the flame retardant risk assessments. However, in such an evaluation of oral exposures, EPA must include the high-end exposure approach with fish consumption rates of subsistence fishers.

Mitigation by Avoidance or Replacement is Not an Option. When at least half of your diet is derived locally, you cannot stop eating that and switch to other foods. This type of mitigation action used in past risk management strategies, i.e., "don't consume more than X amount in Y timeframe," amounts to an unfunded mandate and forced cultural loss which is documented to lead to a range of societal ills that cause economic impact as well. As Ocampo wrote: Many First Nations [Indigenous People] peoples embrace a shared
group identity whose substance is formed not just by one's relationship to the community but also to the land and one's ancestors, which may include plants, animals and other elements of nature. For example, traditional Native Hawai'ians consider the taro, a root staple that nurtures them, a physical ancestor now under their guardianship. Thus, reduction or dispossession of land/loss of stewardship of one's traditional plants and animals is experienced as an alienation or unmooring from the self, and in some
communities is directly correlated with suicide (i.e., among the Guarani of Argentina - see Robinson, 2008).

86	NTTC	1	General, PESS	N/A

Whitbeck, Walls, Johnson, Morrisseau, & McDougall (2009) studied depression and historical loss among Indigenous adolescents, reporting that the measures of perceived historical loss and depression were separate but related constructs. Even when controlling for effecting influences such as family factors, discriminatory treatment, and proximal negative life events, an adolescent's perceived historical loss had independent effects on their depressive symptoms. The construct of historical loss is discussed in terms of Indigenous ethnic cleansing: military defeat, relocation to approximate penal colonies, starvation, neglect, forbidden to practice traditional means of survival and spiritual traditions, forced assimilation, children kidnapped and reeducated in settings that ignored kinship patterns, traditional language use punished, and efforts to replace traditional religious beliefs with Christianity, no specific end to government policies of assimilation, and no acknowledgement of ethnic cleansing or apology for it from the U.S. government. Reinschmidt, Attakai, Kahn, Whitewater, & Teufel-Shone (2016) developed the Stories of Resilience Model from interviewing and documenting Urban American Indian Elders' experiences of historical trauma and resilience. "For Indigenous people removed as children to boarding/residential schools or adopted by White families off reservation, this meant being removed from the tribal lands that were closely tied in with culture and traditions, including subsistence practices (farming and hunting), beliefs (traditional spirituality), and values (having respect for oneself and others). Separation from their families led to a loss of contact with relatives, especially elders, who passed on culture and traditions. Family members could no longer teach Native languages or engage children in family activities."

87	NTTC	1	General, PESS	N/A

Despite these historic and generational traumas, tribes have maintained cultural practices and values, and many tribes—but not all—maintained their Indigenous languages, stories, songs, and millennia of history. Thus, contrary to the efforts of colonization, assimilation, and attempts of genocide, research of Indigenous survivors is demonstrating that traditional spirituality, traditional practices, and cultural identity are proven protective factors for Indigenous children and adults. Further, there is accumulating evidence that traditional spirituality and practices are associated with alcohol cessation, are negatively related to depressive symptoms and suicidal behaviors among adults, and that they are associated with academic success, self-esteem, and prosocial behaviors among adolescents. Reinschmidt et al reference work by Kirmayer, Dandeneau, Marshall, Phillips, & Williamson (2011, 2012) supporting that community resilience is compatible with Indigenous values of relationships among people and with the environment. Distinct notions of personhood, where individuals are connected to the land and the environment, shape Indigenous ideas of individual resilience. “Land plays a critical sacrosanct role: it is itself sacred, with tribal-specific meaning, and it is also often directly connected to ritual sacred sites, where ceremonies and obligations are expected to be fulfilled.” (Walters, Simoni & Evans-Campbell, 2002.)

88	NTTC	1	General, PESS	N/A

Resilience strategies in the context of the community included being “connected to the community,” “involved in local community cultural activities,” and “knowing one’s Native language” were. Another elder’s story demonstrated the connection between personal, family, and community resilience: "think the values that I picked up when I was growing up was making my baskets. That was one of the things that REALLY was good for me... I was taught by my mother and I learned that it really did help me. She ...showed me how to prepare to make basket: first to go out and get the plants... I have to talk to the plants. You go up to the plants while you get them, so that it will help you, strengthen you, give you the courage to go on with your life and it’s really not just making baskets. It’s something that, it’s sort of like a sacred secret. So that’s what I did. I found out that that’s REALLY helped me a lot. Not just making baskets, but keeping up with our tradition, something that our people used to make and use for many things. And also, I sell my baskets a lot so that helped me in many ways...that was my income when I couldn’t work..." The Indigenous notion of personhood connects individuals to larger contexts, including family, community, spirituality and history. As described by the elders in the study, and in the literature (Kirmayer et al., 2009, 2012), the Indigenous notion of the self (or person or individual) is one of connectedness. Individual resilience thus must be understood as systemic in nature, because it refers to Indigenous notions of the individual that are characterized by connectedness. In telling their stories, elders talked about people who served as role models for them, about being role models themselves, and about the importance of role models. Most elders fondly remembered their grandparents, parents, or aunts. These relatives imparted knowledge and skills, including gardening, butchering, counseling others, being medicine men, and knowing traditions around birth and death.

89	NTTC	1	General, PESS	N/A
90	NTTC	1	General, Exposure	N/A

Healing among North American indigenous populations have common themes, shared health beliefs and a unified perspective of bio-psycho-socio-spiritual approaches and traditions, regardless of tribal-specific differences in healing practices, like feathers of different birds, sweat lodge or bonya steam bath, burning a dried herb or burning a fire dish of food. “The culture is the primary vehicle for delivering healing.” Bassett, Tsosie, & Nannauck. 2012) “Native diets, ceremonies that greet the seasons and the harvests, and the use of native plants for healing purposes have been used to live to promote health by living in harmony with the earth.” Koithan & Farrell (2010). Food from the land gives people life and brings them wellness. (Youth Taking Action, no date (n.d.)) "Alaska Natives have been nourished by foods from the land, air, and water for thousands of years (Alstrom & Johnson, n.d.)34. They have had a lifelong association with these foods, seeking them, harvesting them, cleaning them, preparing them to be eaten or stored, keeping the foods safe from loss of spoilage, and enjoying them as foods. People take great comfort from eating the foods they’ve grown up with. These foods can be very comfortable to eat in times of illness and healing, and are very rich in the nutrients necessary for good health. Native foods tend to be very good sources of nutrients like protein, iron, Vitamins A, D and E, and low in saturated fats and sugars. Native foods are the heart of culture and health. They provide close ties to the land and the seasons and the environment. Participating in harvesting, preparing, sharing and eating the foods along with others contributes to spiritual well being."

Disposal pathway regardless must be considered because contamination of media occurs even with best practice and facilities.

91	NTTC	1	General, Exposure	N/A
92	NTTC	1	General	N/A
93	NTTC	1	General, Exposure	N/A

Throughout Asia, non-PBDE BFRs like HBCD, have extensively polluted coastal waters (Isobe, Ogawa, Ramu, Sudaryanto, & Tanabe 2012). They used mussels as a bioindicator, as did studies by the US National Oceanic & Atmospheric Administration of coastal US waters (Isobe et al., 2012), Isobe et al were studying the presence of BFRs, the range throughout Asia, and the levels of concentrations. Among the three HBCD diastereoisomers, α-HBCD was the dominant isomer followed by γ- and β-HBCDs. Concentrations of HBCDs and DBDPE in mussels from Japan and Korea were higher compared to those from the other Asian countries, indicating extensive usage of these non-PBDE BFRs in Japan and Korea. Higher levels of HBCDs and DBDPE than PBDEs were detected in some mussel samples from Japan. The results suggest that environmental pollution by non-PBDE BFRs, especially HBCDs in Japan, is ubiquitous. This study provides baseline information on the contamination status of these non-PBDE BFRs in the coastal waters of Asia. More than 1,500 construction and demolition debris (CDD) landfills operate in the United States (U.S.), and U.S. federal regulations do not require containment features such as low-permeability liners and leachate collection systems for these facilities (Powell, Jain, Smith, Townsend, & Tolaymatl; 2015). Here we evaluate groundwater quality from samples collected in groundwater monitoring networks at 91 unlined, permitted CDD landfills in Florida, U.S. A total of 460,504 groundwater sample results were analyzed, with a median of 10 years of quarterly or semiannual monitoring data per site including more than 400 different chemical constituents. Downgradient concentrations of total dissolved solids, sulfate, chloride, iron, ammonia-nitrogen, and aluminum were greater than upgradient concentrations ($p < 0.05$). At downgradient wells where sulfate concentrations were greater than 150 mg/L (approximately 10% of the maximum dissolved sulfate concentration in water, which suggests the presence of leachate from the landfill), iron and arsenic were detected in 91% and 43% of samples, with median concentrations of 1,900 µg/L and 11 µg/L, respectively. These results show that although health-based standards can be exceeded at unlined CDD landfills, the magnitude of detected chemical concentrations is generally small and reflective of leached minerals from components (wood, concrete, and gypsum drywall) that comprise the bulk of discarded CDD by mass.

In August 2015, EPA published for public comment its TSCA Work Plan Chemical problem formulation and initial assessment documents for the three flame retardant clusters Brominated Bisphenol A (TBBPA), Chlorinated Phosphate Esters (CPE), and Cyclic Aliphatic Bromides (HBCD) (USEPA 2015c). In response NTTC provided written comments to that docket which we recapture here in relevance to problem formulation and risk evaluation under the amended TSCA.

NTTC appreciates EPA's inclusion of fish consumption by subsistence fishers and their children when evaluating exposure pathways for CPE. We specifically highlight EPA's commitment to account for the high-end fish consumption of subsistence fishers—including pregnant women, children and adults—the majority of whom are the tribal population.

94	NTTC	1	General, PESS, Exposure	N/A

With Tribes as a representative population for greater environmental media exposure risk, any resultant action levels will not only protect tribes and the general population, but the ethnic, minority, and rural population groups that may be at higher risk due to their customary lifestyle and activities and/or traditional practices. Fishing illustrates this point. Fishing is a universal practice for Alaska Tribes, potential exposure via ingestion of contaminated fish is higher due to higher consumption, as is potential exposure via inhalation through smoking fish, and other heat preparation methods particularly with poor indoor ventilation, via potential absorption when fishing and preparing a greater amount of fish, via non-dilution of contaminated fish with fish from another location due to unavailability of store-bought fish, via particular practices associated with fishing, which may include gathering greens and using untreated water near the fishing spot, etc. Also, the full Tribal population – from infant to elder, disabled, single parents with small children and relative living outside the village – is exposed due to sharing of fish. This is a magnified representation of the Alaska population as a whole, particularly the rural population, which tend to fish for, and share and eat fish like salmon, at a much greater rate than their counterparts in the contiguous states. The same can be said for exposure to contaminated "game meats", marine mammals, berries, water and other environment sources due to customary food resources and recreational activities. With Tribes as representative, the full Alaska population is protected.

95	NTTC	1	General, PESS, Human Health	N/A
96	NTTC	1	General, PESS, Human Health	N/A

The sociocultural consequences to Tribal communities of overexposure to chemicals are as significant, or more significant, compared to the consequences to other groups. The small population size, high-context, and group-oriented nature of Tribal populations translates to substantial impact on health and well-being when a Tribal member is negatively affected by chemical exposures. For example elders are a significant resource in their community and fill multiple roles. Teachers of cultural values and mores for their community including other older adults that are younger than the elder in addition to children and teens. It is well documented that tribal people's socio-cultural knowledge base is more internalized and is not adequately learned via verbal or written instructions. It must be acquired over a lifetime of experiencing the day-to-day contexts of being a tribal person and relating with elders that have fully acquired the knowledge in their time by being with generations past. Sources of historical information shared with their community including other older adults that are younger than the elder in addition to children and teens. Leaders whose experience provides stability and experience to the tribal council and in consultations with government agencies. Caretakers for extended family members, providing unpaid childcare. A grandmother who develops cancer will not be able to care for her grandchildren, parents may miss work resulting in job or income loss, or children may miss a critical mentor role or be injured because they are left alone.

Impacts to societal health and well-being contribute to disproportionate health and socioeconomic indicators. E.g., exposure to a certain chemical affects childhood brain development, causing neuro-developmental delays, which are compounded as the child progresses through school and Tribal populations suffer from low high school and college graduation rates.

97	NTTC	1	General, PESS, Exposure	N/A
98	NTTC	1	General, PESS, Exposure	N/A

While NTTC recognizes that part of EPA's risk assessment process is collecting existing data on the chemicals in question, asking tribes to fill this data gap is unreasonable. EPA must provide funding before starting the process (at least more than one year prior) to request tribes gather information. Specifically, sampling within tribal homes in high-risk areas would provide valuable data to further complete risk assessments accounting for high-risk, vulnerable tribal populations. EPA must take into account widespread backyard open burning and open burning at both municipal and construction & demolition landfills. Tribal and other rural citizens are exposed to chemicals in commerce via this pathway, including HBCD. These types of burning are prevalent in underserved tribal communities on reservations in the U.S. and other rural lands, including nearly every community in the State of Alaska. These communities rarely have proper burn units nor appropriate safety protocols to prevent residents' inhalation.
Again, regarding fish consumption and the rate referenced above, in relation to population scenarios, the tribal population scenario is the most appropriate to use for risk assessments by EPA, because their rules indicate that they are to protect the population of highest risk. As identified in the 2015 problem formulation for the HBCD cluster, EPA must use fish consumption rates for subsistence fishers in aggregate exposure for those who rely heavily on locally sourced fish.

99	NTTC	1	General, PESS, Exposure	N/A

It is imperative that EPA consider potential cumulative exposure—including multiple chemical exposure—in these risk assessments because it is an on-going void in implementing environmental justice policies. This is a significant problem that EPA is not considering cumulative exposure in the risk assessment process at this time. It is an environmental justice issue affecting tribes, who rely heavily on high volumes of fish and aquatic mammals for half or more of their diet. Additionally, a large percentage of American Indian and Alaska Native communities are at or below the poverty level. This translates to lower replacement cycles of furniture, toys, clothing etc. from those with higher toxicities to more recently manufactured items of lower toxicities. For example, although PCB is no longer manufactured, studies have detected it in Puget Sound tissue sample monitoring. EPA must also look at wastewater outside of only the Toxics Release Inventory, which does not account for small local government facilities like unlined but permitted landfills, unpermitted landfills, open dumps, and open dump and backyard burning. As the Council has previously discussed with EPA, the stovepiped processes of EPA fails in protecting tribes from exposures to chemical in commerce.

Systematic Review - Public Comments on the Application of Systematic Review in TS

FULL LIST OF COMMENTS

#	Submitter	Attachments (#)	Category (RegNex, Editorial, Exposure, Fate, Engineering, Human Health, Eco Health, PESS, Policy, Other, Systematic Review, General)	Document Section #
1	ACC	3	Systematic Review	N/A
2	ACC	3	Systematic Review	N/A
3	ACC	3	Systematic Review	N/A
4	ACC	3	Systematic Review	N/A
5	ACC	3	Systematic Review	N/A

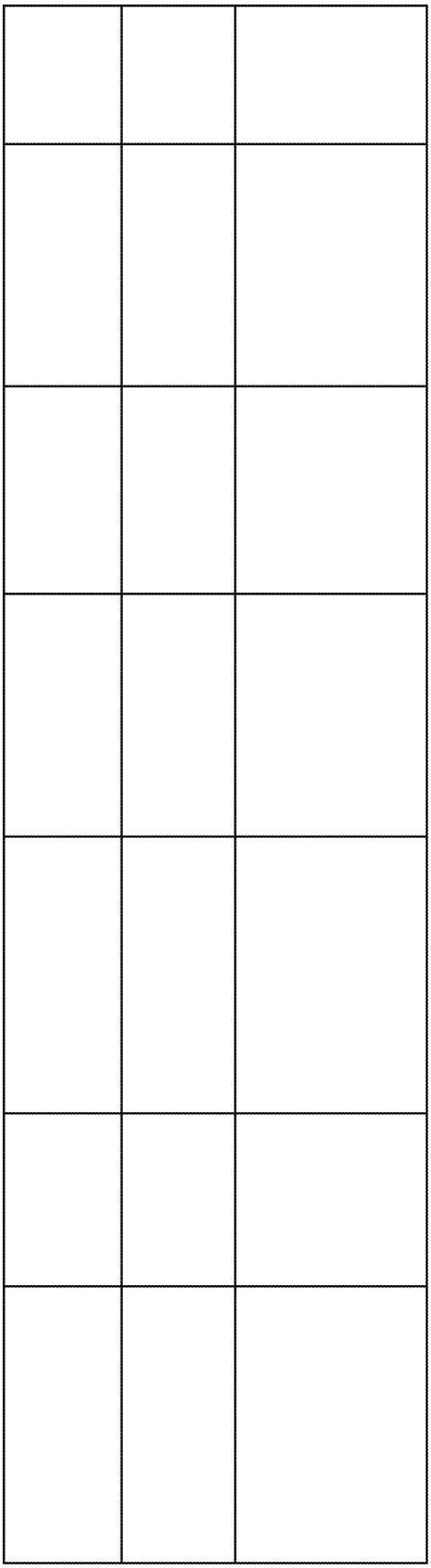
CA Risk Evaluations

Comment
ACC appreciates the transparency and progress toward documentation of the TSCA systematic review approach. EPA has developed a strong baseline systematic review approach, emphasizing the importance of allowing for "fit-for-purpose" evaluations tailored to specific substances and an iterative evaluation process. The guidance outlined for data searches, data screening, and data extraction is comprehensive and useful. Notably, the current guidance has a strong focus on study quality, and thoroughly outlines the proposed steps for study quality evaluation for each domain of evidence.
However, there are some critical systematic review concepts and methodologies that remain to be discussed or fully developed in the current approach document, most notably for the process of evidence integration. Following the consideration of initial comments received, and the further development of the approach in the draft risk evaluations for the first 10 chemicals, EPA should re-issue the systematic review framework document with appropriate updates and allow for additional review and stakeholder feedback. In particular, at that time, EPA should put forward the standardized procedures the Agency will use for integrating evidence that ensures consistent use of best available science, weight of the scientific evidence, and, as applicable, an understanding of mode of action (MOA).
The systematic review process should have sufficient flexibility such that it can adapt to the realities of the chemicals being tested and the limitations in experimental methodology and laboratory techniques. For example, the challenges in collecting hazard, fate, and exposure data for chemicals with any one of a number of characteristics which make them “difficult substances” for testing purposes are well known. Results from common adaptations of typical test methods for difficult substances should not be blindly rejected but should be subject to expert judgment to confirm the validity and applicability of such data.
EPA should add discussion emphasizing the importance of incorporating information on MOA data in problem formulation, and consider organizing the problem formulation step around these data, even if the MOA is not entirely clear from the outset. Existing frameworks, such as the World Health Organization (WHO)/International Program on Chemical Safety (IPCS) MOA/Human Relevance (HR) Framework, the Adverse Outcome Pathway (AOP)framework, or other similar approaches may be useful.
Within the problem formulation phase of the evaluation, EPA must clearly describe any decisions regarding its planned use of other EPA office or agency assessments of the chemical under review. Further, OPPT should not automatically adopt existing toxicity criteria in the absence of its own review and consideration of possible alternative values using the proposed systematic review approach.

RAD POC	Docket #	Action Needed

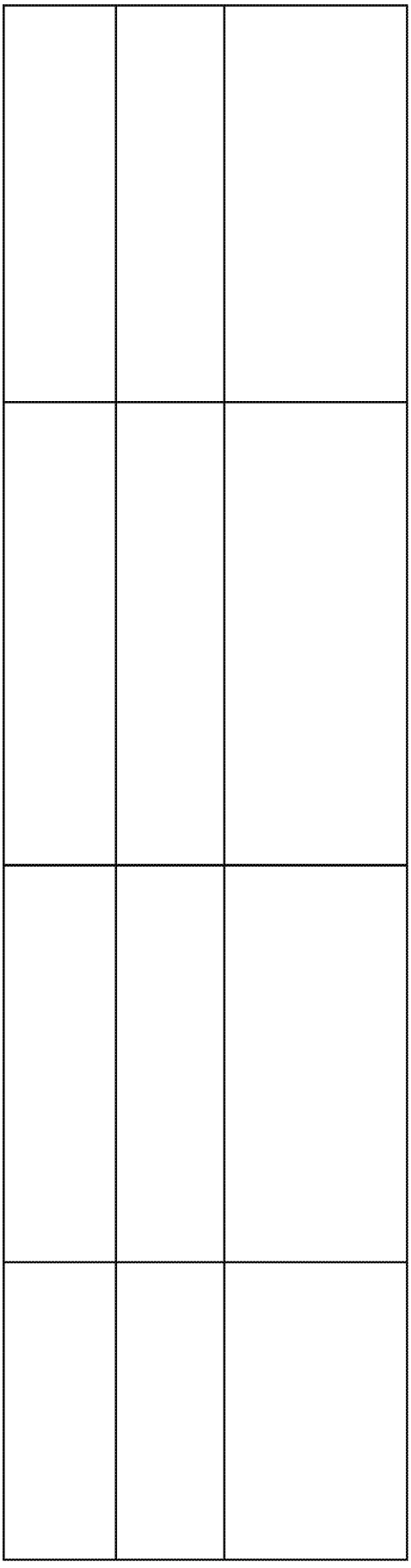
6	ACC	3	Systematic Review	N/A
7	ACC	3	Systematic Review	N/A
8	ACC	3	Systematic Review	N/A
9	ACC	3	Systematic Review	N/A
10	ACC	3	Systematic Review	N/A
11	ACC	3	Systematic Review	N/A
12	ACC	3	Systematic Review	A.1

We support EPA's intention, as specified in the problem formulation documents, to conduct its own independent assessment of existing toxicity values. In many cases, these existing reviews are dated and were published without the benefit of systematic review and consideration of available studies reflecting the best available science that have been more recently developed.
Regarding the data collection phase, the current approach for data searching, screening, and extraction is well developed. EPA provides detailed information on its plans to use specific search strategies and databases, how decisions will be made regarding screening (in both the abstract/title and full text screening phase), and how it will carry out the quality assurance (QA)/quality control (QC) process for all three parts of data collection. Further, EPA includes example search and screening strategies used for the first 10 chemicals, which provide helpful context on the implementation of this phase of the risk evaluation.
EPA's consideration of grey literature, such as technical reports, conference proceedings, and unpublished industry data, is well supported, as there are many sources that may be useful that have not been published in peer-reviewed journals. In order for this approach to be truly fit for purpose, it is critical that EPA capture studies generated for regulatory purposes at the data collection stage. EPA should also consider the possibility of publication bias in the peer-reviewed literature; i.e., the possibility that studies with negative findings may not have been published.
ACC supports EPA's recommendation that the Agency pilot test the search and screening methods, which will be important for iterative evaluations. This will allow for changes to be made if it becomes clear that references have been missed by the use of specific search terms, or if relevant articles are being unintentionally screened out. Further, it is critical that EPA thoroughly describe the reasoning for any changes to risk evaluations resulting from pilot testing or other iterative phases of the assessment. Clarification is also needed as to how EPA will carry out iterative methods in later phases of an evaluation.
Overall, the systematic review approach covers essential aspects of evaluating study quality. It indicates that EPA intends to thoroughly evaluate and fully consider the implications of the quality and relevance of the available evidence before incorporating it into its risk evaluations. There are many positive attributes in the methods EPA describes, such as a training phase for reviewers to ensure consistency across quality evaluations. The specific criteria are informed by several existing, well-regarded evaluation systems that detail critical study quality and reporting criteria systems, such as the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement and the Biomonitoring, Environmental Epidemiology, and Short-lived Chemicals (BEES-C) instrument.
The study quality evaluation process appears to be very time intensive, and it is unclear whether it is possible to complete it in full for every evidence type for each evaluation, given the tight regulatory deadlines under TSCA. It is also unclear whether, as an alternative, EPA may rely on existing quality evaluations, and, if so, how these evaluations will be evaluated to ensure they adequately fulfill the rigorous quality assessment requirements proposed for TSCA evaluations.
Page 33 of the systematic review approach states, " EPA/OPPT plans to use data with an overall quality level of High, Mediu, or Low confidence to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated as Unacceptable." ACC agrees that unacceptable data should not be used in the risk evaluation.There is some concern that low confidence studies could be used to quantitatively support a risk evaluation. If there is low confidence in the study methods and/or reporting, then it should not be used to quantitatively support the derivation of a point of departure in a hazard assessment. Rather, it should be used qualitatively as a supporting study or in a weight-of-evidence determination for hazard characterization.



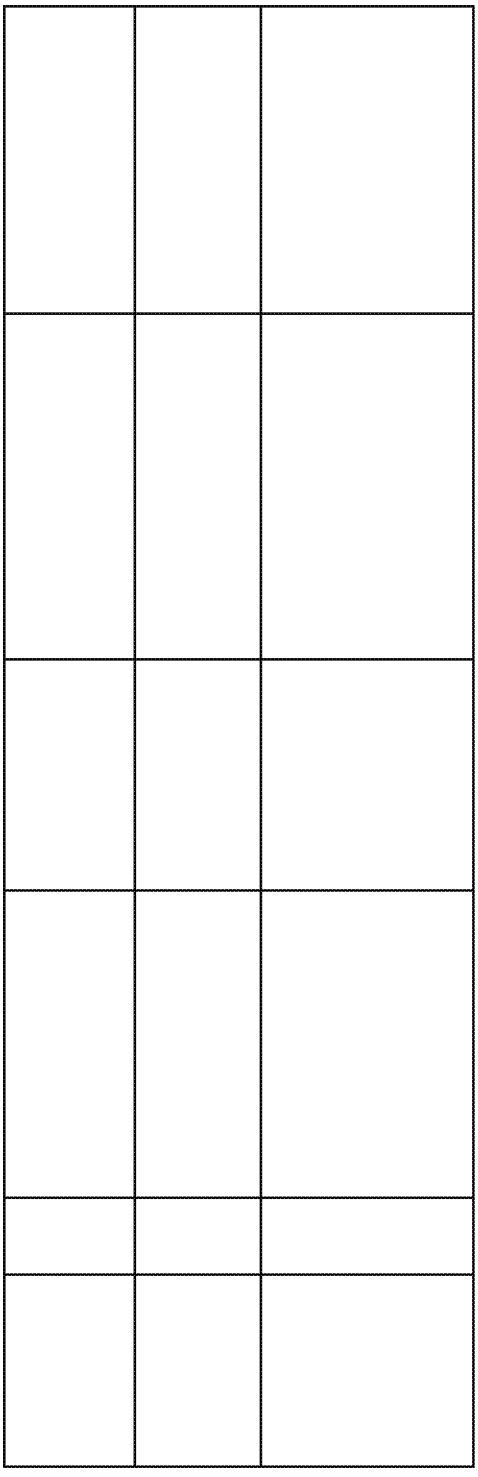
13	ACC	3	Systematic Review	Appendix A
14	ACC	3	Systematic Review	Appendix A
15	ACC	3	Systematic Review	Appendix A
16	ACC	3	Systematic Review	N/A

EPA states that it will not automatically assign lower confidence to studies not adhering to Good Laboratory Practice (GLP) or Organisation for Economic Co-operation and Development (OECD) guidelines, but rather, it will consider, "any and all available, relevant data and information that conform to the TSCA science standards" as acceptable. What this might mean for academic studies, which are usually not conducted according to GLP requirements and may use non-standard methods, is unclear. EPA should ensure that the study quality evaluations retain consideration of the robust and highly documented process required by GLP guidelines, even if they are not GLP studies. As noted by Borgert et al., 2016, "...regulatory agencies have placed a high value on study reports that include sufficient detail to allow reanalysis of data to independently confirm results and support additional analysis using alternative methods of data evaluation." Borgert and co-authors also emphasize that GLP-compliance is much more than record keeping and reporting.
Overall, the scoring examples shown are clearly and transparently laid out in a series of tables. The weighting scheme, metrics, and overall scoring are relatively straightforward.ACC appreciates EPA's intention to be highly transparent and consistent in its evaluations through the use of a quantitative study scoring system. However, the scoring system described in the current approach is complicated by many possible options that may or may not be used, such as weighting factors. This may result in very specific scores with a relatively narrow range, which may make interpreting studies of similar but not identical quality difficult (e.g., a score of 1 versus 1.7). Further, some of the weighting factors chosen involve substantial scientific judgment, and EPA should consider that some metrics may be more important to overall quality for specific studies, relative to others, indicating that a generic "one-size-fits-all" weighting factor could become problematic. For example, in the criteria for occupational exposure and release data evaluation, it is unclear why the metric of methodology in the reliability domain is given a weighting factor of 1, when other critical factors, such as reliability, are weighted at 2. Incorrect or inappropriate methodology could be just as critical of a flaw, if not more so, than some of the other metrics.
In addition, while the use of a 1-4 scale for judging whether a study is evaluated to have high confidence, medium confidence, low confidence, or be unacceptable for use is clearly laid out and justified, it is anticipated that there could be some confusion with the already much-used Klimisch system of study evaluation.18 The Klimisch system is somewhat similar in that studies assigned a 1 or a 2 are considered reliable without restrictions, or reliable with restrictions, respectively. However, the Klimisch system differs from the one EPA is proposing by attributing a score of 3 to studies that are not reliable, and a score of 4 designating a score is not assignable due to insufficient information. In other words, the scale used on EPA's approach is the opposite of the Klimisch system for scores of 3 and 4. Furthermore, Klimisch scoring does not use weights or calculate mathematical averages, but rather assigns qualitative overall integer values of 1, 2, 3, and 4. Since the Klimisch scoring is already broadly used in regulatory activities across the globe, EPA should consider harmonization for evaluating studies in order to avoid confusion and harmonize with other geographies.
The availability of data and other information required to verify and reproduce critical studies in the risk evaluation is also important. Any data that are used to derive toxicity criteria should be made publicly available to the greatest degree possible, while still protecting confidential business information (CBI) and other sensitive personal information, consistent with EPA's recently proposed rule on Strengthening Transparency in Regulatory Science. This will facilitate transparency and allow others to consider and independently evaluate the quality, reliability, and interpretation of these data. For example, a frequent concern with published academic studies is that the data presented in either tabular or figurative form have already experienced some form of statistical transformation. In many cases, even an expert-level statistician cannot recreate the original data from these data.



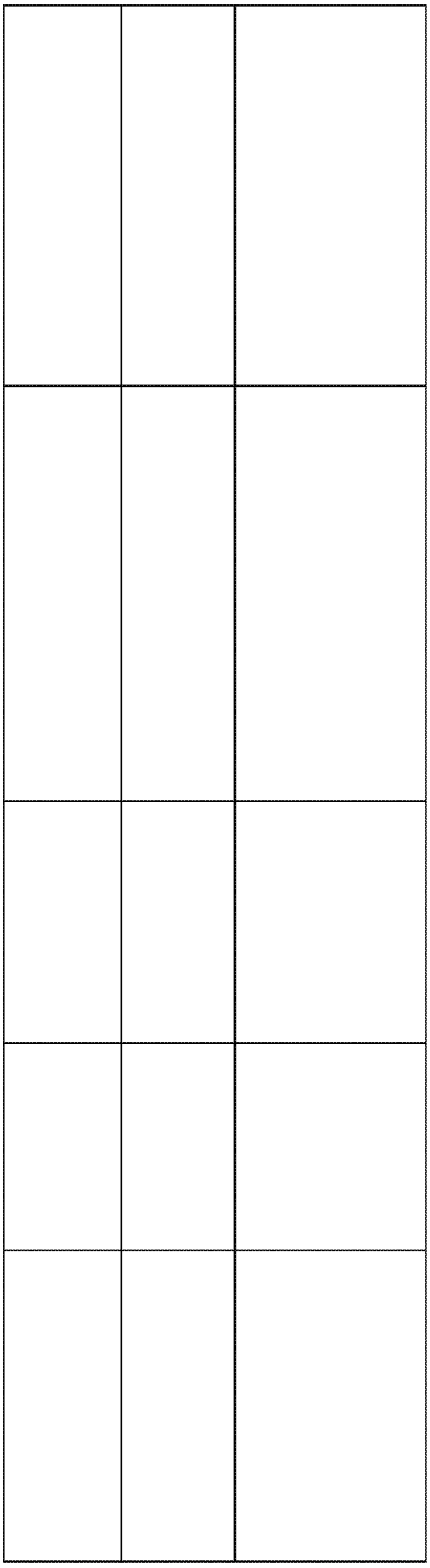
17	ACC	3	Systematic Review	N/A
18	ACC	3	Systematic Review	3.4
19	ACC	3	Systematic Review	3.4
20	ACC	3	Systematic Review	3.4
21	ACC	3	Systematic Review	3.4
22	ACC	3	Systematic Review	3.4

Academic laboratories sometimes conduct their statistical analysis using laboratory personnel who are not professional statisticians. The technical issue with non-professional analysis is rarely whether the test was conducted correctly, but rather whether the most appropriate statistical test was selected. In a seminal study conducted by Begley and Ellis (2012), the study authors were unable to replicate the results from statistical analyses of 47 of 53 landmark pre-clinical cancer research papers. This led to a flurry of other studies in different fields that have also reported similar findings. Thus, it is crucially important that data upon which regulatory actions are based be available for independent statistical analysis.
In the current systematic review approach document, the strategy for evidence integration lacks detail and specificity. Only general, high-level principles are described, and no specific weight-of-evidence methodology is presented as a baseline for TSCA assessments. EPA recognizes that the evidence integration phase of assessments is underdeveloped and indicates that it anticipates defining and demonstrating the process of integration in the forthcoming first 10 chemical draft risk evaluations. We expect that as EPA gains more experience with evidence integration, and can describe the standardized procedures the Agency will use for integrating evidence that ensures consistent use of best available science, weight of the scientific evidence, and, as applicable, understanding of MOA, the Agency will revise this guidance document. Such a revision should include additional review and public comment.
First, EPA should use a transparent process to integrate evidence that is standardized in such a way to allow for greater efficiency. EPA should consider development of a structured narrative that fully describes how the different pieces of available evidence support a given conclusion/argument or an alternative. In this way, EPA can clearly demonstrate how specific studies or data sources contributed to the final conclusion. This will ensure that the process by which EPA reaches conclusions about exposure, hazard, and/or risk will be well developed and transparent.
Second, as a part of the evidence integration narrative, EPA should clearly describe how the study quality evaluations will be used to weigh the evidence and reach conclusions for the different phases of the risk evaluation, including exposure assessments, hazard assessments, and any quantitative estimates of risk. For example, the current approach does not indicate whether a high-confidence study will always be given more weight than a medium-confidence study in formulating conclusions, or how other factors, such as study relevance, will be weighed with quality considerations. EPA should consider building from the published approaches for quantitative weight-of-evidence analysis, such as Bridges et al., 2017; Becker et al., 2017; and Dekant et al., 2017.
Third, EPA should detail how it will conduct uncertainty analyses and communicate these uncertainties consistently and transparently in each risk evaluation.
While MOA/AOP evidence and mechanistic data are mentioned in several places in the systematic review approach, EPA should consider expanding its discussion of this important evidence, particularly in the evidence integration phase of evaluation. MOA/AOP evidence and mechanistic data should be weighed concurrently with observational and toxicology evidence and considered a critical organizing principle for the weight-of-evidence evaluation.



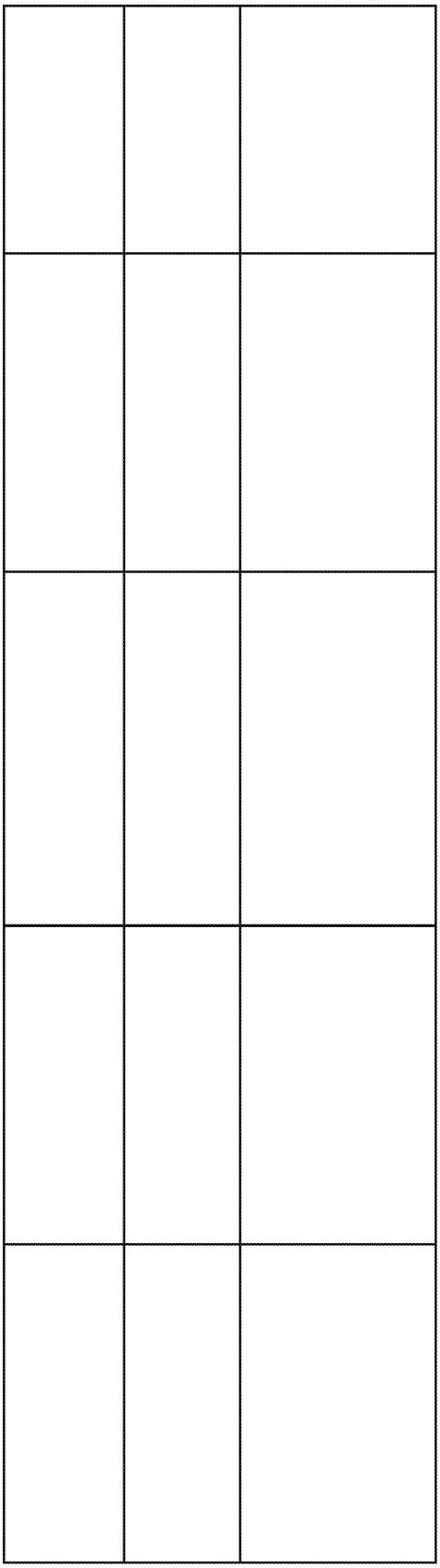
23	ACC	3	Systematic Review	3.4
24	ACC	3	Systematic Review	3.4
25	ACC	3	Systematic Review	3.4
26	ACC	3	systematic Review	3.4
27	ACC	3	Systematic Review	3.4

The AOP framework can be employed specifically as an organizing principle that explains MOA and the connections to adverse outcomes. The AOP framework is a tool to systematically organize available data and knowledge that describes scientifically plausible and causal relationships across multiple levels of biological organization between a molecular initiating event (MIE) and subsequent key events (KEs), culminating in an adverse outcome (AO) potentially relevant to risk assessment. EPA researchers have been instrumental in developing AOPs and tools to facilitate the further development, review, and use of AOPs in scientific and regulatory endeavors. Tools such as the AOP wiki can be mined for additional data and organizational principles as well as domains of applicability for various identified MOAs associated with chemicals. Thus, whether evidence generally aligns or does not align with any proposed or known MOAs and/or AOPs should be a necessary consideration in integrating evidence to reach conclusions.
Since the scientific justification for assessing human relevance and selecting dose-response extrapolation methods for quantifying potential cancer risks at environmentally relevant levels of exposure is highly dependent upon the determination of the likely operative MOA, the Agency should implement a systematic and explicit approach for evaluating a chemical dataset, using hypothesized MOAs and the evolved Bradford Hill causal considerations, to integrate evidence and derive weight of the evidence confidence scores for potentially relevant MOAs. This approach enables a side-by-side comparison of numerical weight of the evidence confidence scores for different hypothesized MOAs, including the default linear no threshold model. This enhances transparency and improves communication among risk managers and the public. This best available science approach provides a transparent, scientifically sound justification for using the most likely operative MOA as the basis for selecting the most appropriate extrapolation method to then calculate potential risks to humans for environmentally relevant exposures.
In addition, EPA should describe how it will consider issues of the adversity of identified health effects when considering the weight of the evidence. For example, there may be animal studies that demonstrate statistically significant effects that are reversible, and/or epidemiology studies may show changes in blood biomarkers but are not predictive of clinical disease. Results of this nature (those for which the adversity or clinical relevance is either questionable or unclear) should be interpreted with caution when making causal conclusions regarding hazard, and when selecting endpoints for consideration as critical effects.
Finally, EPA should add a discussion of how it will consider questions of relevance in the data evidence integration and summary phases of the risk evaluation. EPA indicates that it will use a tiered approach to check for relevance at various points in each risk evaluation, including during data screening and selection. However, it is not entirely clear how data will be weighed according to relevance when integrating evidence to support conclusions when presumably, at this point in the evaluation, all evidence discussed was previously deemed relevant to the risk evaluation for some purpose.
EPA should consider reviewing and adapting portions of other established systematic review and weight-of-evidence frameworks. For example, one recent and generally well-developed framework is the European Food Safety Authority (EFSA) Guidance on the use of the weight-of-evidence approach in scientific assessments.30 Critical concepts in weight-of-evidence are well described, including the consideration of relevance, reliability, and consistency within and across lines of evidence. Various options for causal frameworks are presented, and EFSA emphasizes that, in many cases, a single method often cannot cover all steps. Differing methods, or a combination of methods, may be needed for a given assessment. These fit-for-purpose decisions can be documented in the problem formulation phase of assessment and thus will be vetted via peer review and public comment.



28	ACC	3	Systematic Review	3.4
29	APHA	1	Systematic Review	N/A
30	APHA	1	Systematic Review	N/A
31	APHA	1	Systematic Review	N/A
32	APHA	1	Systematic Review	N/A

Transparency in the decision-making process is vital for producing scientifically defensible and understandable assessments. Clear, thorough discussions of all decisions will increase confidence and aid in the general acceptance of the findings and conclusions of TSCA risk evaluations. The transparency of overall conclusions on chemical hazard, exposure, and risk may also be enhanced by the use of tabular and/or graphical summaries of the weight-of-evidence conclusions. Further, it is important that in all phases of the assessment, but particularly in the evidence integration and summary sections of the assessment, EPA clearly describes all areas in which expert judgment was utilized.
In addition, the Systematic Review Guidance describes how the agency intends to identify, evaluate, and integrate scientific information for TSCA risk evaluations. The guidance will be pivotal to the conduct and ultimately the scientific credibility of these evaluations. Yet the guidance is inconsistent with the best available science and has not been peer reviewed by independent experts. The current draft diverges from established techniques in use in the scientific community. I urge the agency to comply with its own Peer Review Handbook, to arrange for peer review of the guidance by the National Academy of Science, and to revise the guidance based on the results of this peer review prior to relying upon it to conduct systematic reviews for TSCA risk evaluations.
EPA's Systematic Review Guidance describes how EPA intends to identify, evaluate and integrate scientific information used in TSCA risk evaluations. The guidance will shape, for example, whether and to what extent the agency considers a study finding that exposure to a chemical was associated with a particular adverse health effect. TSCA requires EPA to "use scientific information, technical procedures, measures, methods, protocols, methodologies, or models, employed in a manner consistent with the best available science" and to "consider as applicable...the extent of independent verification or peer review of the information or of the procedures, measures, methods, protocols, methodologies, or models." § 26(h) (emphasis added). Yet the guidance is not consistent with the best available science nor has it been peer reviewed by independent experts. EPA's reliance on this version of the guidance would violate TSCA.
The guidance is not consistent with best practices for systematic review. The guidance includes hundreds of pages of data quality criteria that EPA will use to assign numeric scores to individual studies. The agency says it may disregard a study based on the numeric score assigned to it. This is an outdated approach. NAS discourages the use of numeric scoring in systematic review, noting that "[i]n recent years, systematic review teams have moved away from scoring systems to assess the quality of individual studies," in part because scoring systems have not been validated and different systems can produce radically different results. Notably, systematic reviews conducted by EPA's Integrated Risk Information System do not utilize numeric scoring, and neither should systematic reviews conducted under TSCA.
Surprisingly, EPA has not subjected the guidance to peer review. This is a major omission. In addition to ignoring TSCA's requirement to consider the extent of peer review of the scientific information and technical procedures used by the agency, relying on the guidance when it has not been peer reviewed would harm the scientific credibility of the TSCA program. As EPA's own Peer Review Handbook states, "Peer review enhances the credibility and acceptance of the decision based on the work product," which in this case is the decision to regulate or not regulate a chemical under TSCA based on a risk evaluation and determination. EPA should seek peer review of the guidance by NAS, which has published several reports on the conduct of systematic review for chemical exposure and its application by federal agencies.



33	API	1	Systematic Review	N/A
34	API	1	Systematic Review	N/A
35	API	1	Systematic Review	N/A
36	API	1	Systematic Review	N/A
37	API	1	Systematic Review	p.35
38	API	1	Systematic Review	N/A

API supports EPA's efforts to develop a Policy for Systematic Review in TSCA Risk Evaluations that is consistent and that increases transparency and reduces regulatory uncertainty for stakeholders. API recognizes several positive aspects of OPPT's Systematic Review Policy. The Policy is guided by problem formulation and is based on the best available science and a weight-of-the-evidence (WOE). An emphasis is placed on evidence quality to ensure a quality review. There is a proposed pilot test of criteria for title and abstract screening and tagging. Emphasis is also placed on human health and ecological toxicity testing data meeting minimum reporting criteria (which are necessary for evaluating study quality) and alternative approaches are included. API recognizes that systematic review should, in theory, increase transparency and reduce regulatory uncertainty for stakeholders. API has considered this draft Policy in the context of other established metrics for study quality and approaches to systematic review and has also identified aspects of this draft Policy that would benefit from further clarification.
1. EPA/OPPT's quantitative data evaluation method appears to differ from other established methods and also from the qualitative, yet structured approaches used by EPA/IRIS and others. It is unclear how feasible it will be in practice and the impact on risk assessments.
EPA/OPPT's quantitative data evaluation method appears different from other established methods such as the Klimisch scoring system, OECD guidance for (Q)SAR models3, the Criteria for Reporting and Evaluating Ecotoxicity Data (CRED), etc. The quantitative data evaluation method (individual metrics and domains) for different kinds of data results in apparent inconsistencies, examples of which are provided in point 2) below. The draft Policy is also unclear on how the study scores will be used in the evidence integration and WOE evaluation. For example, it is unclear if a quality weight risk measure will be calculated or if results will be stratified by score. Clarifying information on how quality scores will be used in this draft Policy or in future science policy documents would be helpful in this regard.
API notes that the use of a quantitative approach by EPA/OPPT is inconsistent with a trend toward using more qualitative, structured approaches used by EPA/IRIS and as described in the ROBINS-I tool for assessing bias and in the Cochrane GRADE Handbook. The structure of these more qualitative approaches allows greater latitude for expert judgement without necessarily sacrificing transparency and reproducibility.
EPA/OPPT states as an Important Caveat that "The weighting approach for some of the strategies may need to be adjusted as EPA/OPPT tests the evaluation method with different types of studies." (Page 35). Based on this statement, it does not appear that EPA/OPPT has tested this quantitative data evaluation method on historical data to determine how feasible it is in practice and how it may impact risk assessments conducted under TSCA. Thus, the efficacy and practicality of this approach seem largely unknown, although there are some foreseeable challenges. One foreseeable challenge is how studies that score the same and yet support different very conclusions will be resolved. Another foreseeable challenge is reproducibility in study scoring, both within EPA and externally if stakeholders undertake their own scoring exercises based on EPA criteria. Reproducibility becomes particularly important if differences in study scoring could substantively impact critical aspects of a risk assessment (e.g., endpoints, exposure levels, etc.). These and other foreseeable and unforeseeable challenges could require that the approach be dramatically adjusted such that the final working version is very substantially different from the current draft. To the extent that study scoring impacts risk assessments, there may be inconsistencies in risk assessments as the draft Policy evolves.
2. EPA/OPPT's quantitative data evaluation methods appear inconsistent

39	API	1	Systematic Review	p.32
40	API	1	Systematic Review	p. 76
41	API	1	Systematic Review	N/A

EPA/OPPT's quantitative data evaluation methods appear inconsistent. The draft Policy states:
"The TSCA evaluation strategies in some cases refer to study guidelines along with professional judgement as a helpful guidance in determining the adequacy or appropriateness of certain study designs or analytical methods. This should not be construed to imply that non-guideline studies have lower confidence than guideline or Good Laboratory Practice (GLP) studies. EPA/OPPT will consider any and all available, relevant data and information that conform to the TSCA science standards when developing the risk evaluations irrespective of whether they were conducted in accordance with standardized methods (e.g., OECD test guidelines or GLP standards)." (Page 32).

This implies that studies will not be excluded simply because they are not guideline and/or GLP and that non-guideline/non-GLP studies can rate quite highly if they meet certain criteria. The draft Policy is inconsistent in the degree to which adherence to, or consistency with, standard methods or test guidelines impacts the metrics for particular kinds of data/information. For some kinds of data/information, adherence or similarity to standard methods is required to achieve a high rating (and example of this is monitoring data[7]). For others (e.g., animal and in vitro toxicity data), test guidelines are either not mentioned and appear to be instead substituted with metrics that contain elements similar to those contained in guideline studies (animal toxicity data)[8] or consistency with guideline studies is used as an indicator of quality (in vitro toxicity data)[9]. When test guidelines are available for both animal and in vitro toxicity studies, it seems inconsistent that adherence to or consistency with a guideline would impact study metrics for in vitro studies but not animal studies.

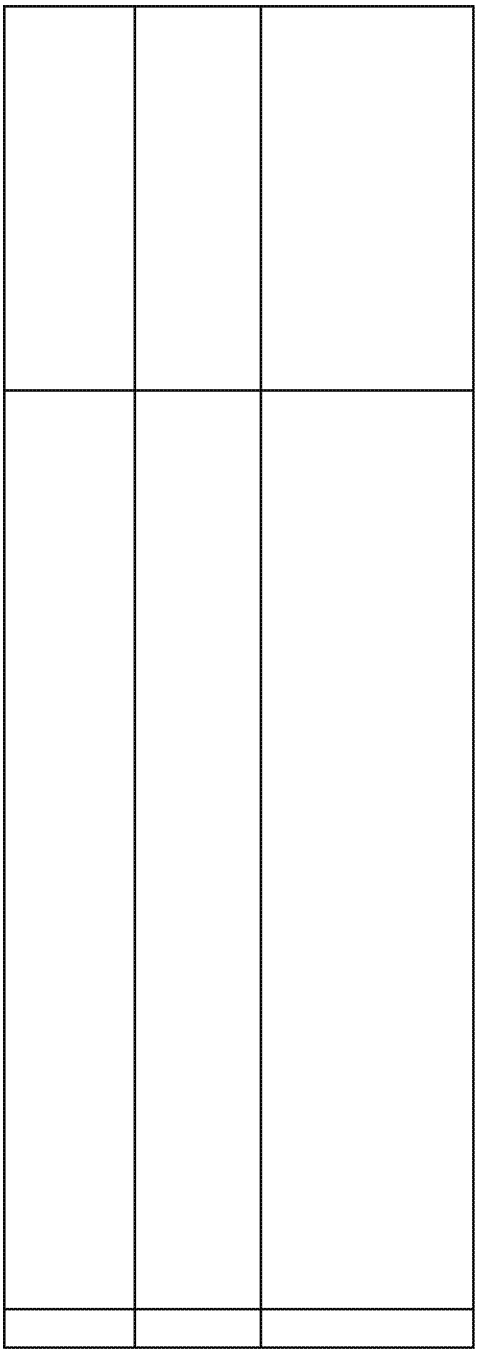
Footnotes:

[7]Table D-11, Evaluating Criteria for Monitoring Data states that "Sampling or analytical methodology is an approved OSHA or NIOSH method or is well described and found to be equivalent to approved OSHA or NIOSH methods" in order to achieve the highest Confidence Level (Score=1) under Domain 1. Reliability (Page 76).

[8]Test guidelines are not mentioned in the Table G-14 Data Quality Criteria for Animal Toxicity Studies, even though numerous test guidelines for animal toxicity studies are available. Instead, study elements commonly addressed in test guidelines and GLP studies appear to have been included as data quality criteria, although this inclusion may not be comprehensive.

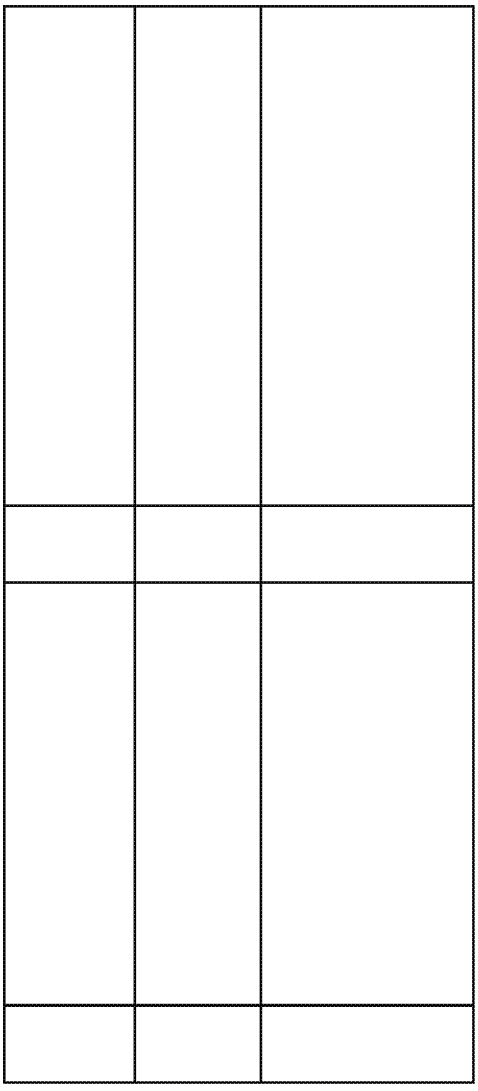
[9]Table G-16, Data Quality Criteria for In Vitro Toxicity Studies, consistency with current standards and guidelines can impact Confidence Level scores in several areas (e.g. Metrics 7,11,15, and 23).

3. It is unclear if EPA will still require studies that are guideline/GLP under TSCA.



42	API	1	Systematic Review	N/A
43	API	1	Systematic Review	N/A
44	API	1	Systematic Review	N/A
45	API	1	Systematic review	N/A

As already mentioned in 2) above, it seems clear that EPA will consider studies that conform to TSCA science standards regardless of if they are guideline/GLP. Some elements of guideline studies appear to be captured in study metrics. However, API was unable to identify any study metrics that captured elements of GLP studies, such as provisions for EPA to access/audit raw data or quality assurance requirements that includes recordkeeping, instrument calibration, and study conduct by persons with appropriate education, training, and experience. Although non-GLP studies may very well have some or all of these benefits, providing these is voluntary, whereas for GLP studies doing so is required. GLP studies done according to established test guidelines add significantly to the cost of research but have historically been considered high quality data for regulatory use and have been required by EPA. The statement above indicates that this may no longer be the case and that regulatory acceptability and use of studies by EPA will now be determined more by compliance with the TSCA evaluation strategies described in this draft Policy than by adherence to test guidelines and GLP. Clarification regarding whether or not this is the case may assist stakeholders in decisions regarding future study design.
4. EPA/OPPT's quantitative data evaluation method may be problematic for complex substances such as UVCB Substances.
The test substance identity and characterization criteria (as currently written) may pose challenges for UVCB Substances and result in a review that scores a UVCB with low confidence based on the current descriptions provided in the evaluation criteria tables. For example, some of the criteria described place modeled data as "low" quality when "Data are estimated (modeled) for the subject chemical substance" and measurement is required for a high data quality rating. However, no provisions are made in the criteria for the use of models that are well accepted. Additionally, in Table C-10, the draft Policy specifies a High Score for metric 1: Test substance identity when "The test substance was identified definitively" (including identification by CASRN) "and the specific form characterized, where applicable". A footnote or short explanation that addresses UVCBs is suggested in order to prevent reviewer confusion regarding the phrase" and the specific form characterized, where applicable" because UVCBs would ikely be exempt as there is no sepcific form to characterize.
5. EPA/OPPT's quantitative data evaluation method may be problematic for the "Up-and-down" procedure and other '3R' (reduction, refinement, replacement) methods.

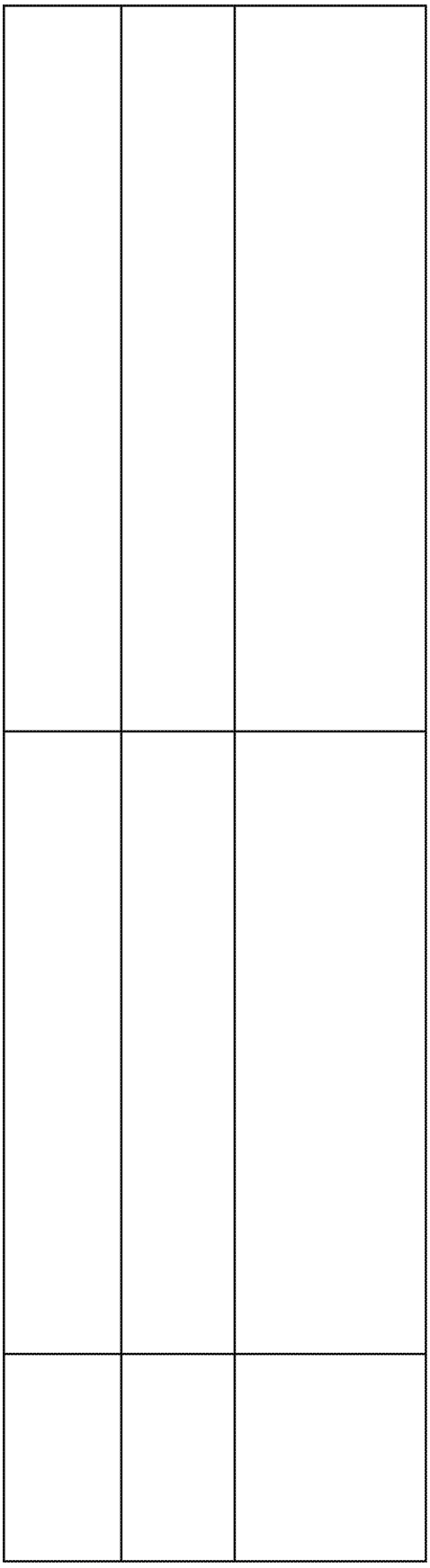


46	API	1	Systematic review	N/A
47	EDF	1	Systematic Review	N/A
48	EDF	1	Systematic Review	N/A

In Table G-13, Serious Flaws that Would Make Animal Studies unacceptable , for the Domain/Metric of Test organisms/Number of animals per group, the draft Policy states that the following would be a Description of Serious Flaw(s) in Data Source: " ... the number of animals per study group was insufficient to characterize toxicological effects (e.g., 1-2 animals in each group). As currently written it seems possible that studies that use the '3R' methods that reduce animal use could be regarded as having a serious flaw under this draft policy. Many of these '3R' methods are supported by analyses that compared the results of the '3R' method to those of the classical test that uses more animals and have been determined perform similarly. This is the case for the "Up-and-Down" proceure for acute oral toxicity tests (Bruce 1987, Yam et al. 1991, Lipnick et al. 1995). A situation in which few animals per dose group and overall are used (in what could technically be regarded as an underpowered study), yet which is bolstered by additional analysis and evidence of similar performance is arguably different for a situation in which a study is underpowered without any additional supporting analyses to indicate that the results would still be reliable. API notes that EPA currently accepts the "Up-and-Down" procedure for acute oral toxicity tests even though only one animal per dose group may potentially be used, and that "It replaces the traditional aacute oral toxicity test formerly used to characterize industrial chamicals, pesticides, and their mixtures." API could find no language in the draft Policy that exempts guideline studies from this metric that use reduced numbers of animals per dose group in a manner that is in accordance with pre-existing EPA science policy. Such languange would serve to provide clarity to both EPA staff and stakeholders on this issue, as well as to further the use of new approach methodologies (NAMs) as described in the 22 June 2018 "Starategic Plan to Promote the Develoipment and Implementation of Alternative Test Methods Within the TSCA Program" (EPA-740-R1-8004).

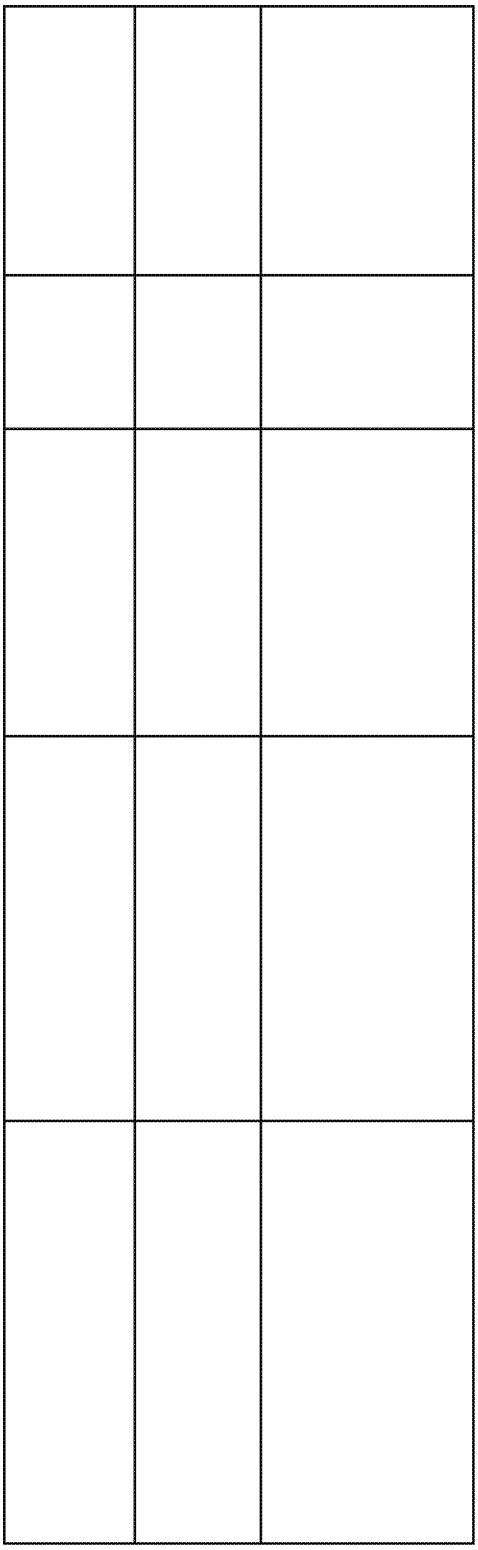
In May 2018, EPA's Office of Chemical Safety and Pollution Prevention (OCSPP) released its Application of Systematic Review in TSCA Risk Evaluations (hereafter "TSCA systematic review document"). This document provides details regarding the Office of Pollution Prevention and Toxics's (OPPT) development of a proposed "systematic review" approach, and the application of this approach to chemical risk evaluations under the Toxic Substances Control Act (TSCA). EPA states that it will apply this approach to the first ten chemicals undergoing risk evaluation under TSCA. OPPT indicates that it has developed a systematic review approach in order to meet the TSCA requirement that "EPA use data and/or information (hereinafter referred to as data/information) in a manner consistent with the best available science and that EPA base decisions on the weight of the scientific evidence." (p. 14) In the final rule Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, the agency defines weight of the scientific evidence as "a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance." In addition to being required by the agency's risk evaluation rule, applying a systematic review framework to chemical risk evaluation is consistent with the recommendations of the National Academy of Sciences (NAS) and leading chemical assessment initiatives across government and academia.

However, the process that OPPT has outlined in this document omits key aspects of what is entailed in a systematic review – even by the agency's own definition. Among other aspects of systematic review that are missing, the TSCA systematic review document does not describe a general approach to protocol development or data integration. To be consistent with the systematic review, EPA should have developed a protocol for each chemical undergoing risk evaluation. EPA has not developed protocols for any of the first 10 chemicals undergoing risk evaluation.



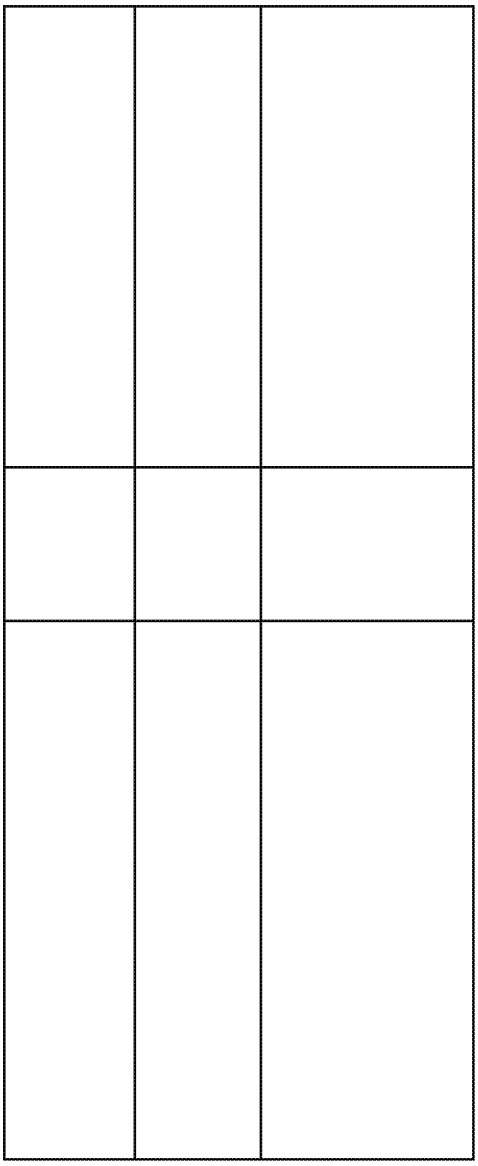
49	EDF	1	Systematic Review	N/A
50	EDF	1	Systematic Review	N/A
51	EDF	1	Systematic Review	N/A
52	EDF	1	Systematic Review	N/A
53	EDF	1	Systematic Review	Pp.75-76, 79-80, 86-87

Additionally, the one aspect of systematic review OPPT has addressed – evaluation of individual study quality – deviates in several significant ways from established best practices in systematic review. EPA has not provided any empirical evidence or other justification for why these deviations are reasonable, necessary, or scientifically sound. Indeed, EPA has provided no indication that it has even attempted to test its approach on a robust set of actual studies to determine what effect its approach to individual study evaluation will have on study inclusion, evidence integration, and the risk evaluation process more generally.
In sum, the TSCA systematic review document deviates significantly from best practices in systematic review—practices that are empirically based and have been scientifically reviewed, vetted, and instituted by other agencies and authoritative scientific bodies. EPA should substantially revise its TSCA systematic review document and subject it to peer review by qualified external experts in the field.
EPA's proposed approach will lead to violations of EPA's science obligations under TSCA § 26(h), (i), and (k). These directives require that EPA must consider all reasonably available information, and that EPA then must make decisions reflecting the "best available science" and "weight of the scientific evidence" based on the body of evidence as a whole. EPA's proposed approach erroneously tries to apply these directives at the level of individual studies, and the result is that EPA may exclude reasonably available information on the grounds that an individual piece of evidence is somehow imperfect, even when it contributes to the "best available science" or adds to the "weight of the scientific evidence" when available information is considered as a whole.
These statutory commands in TSCA repeatedly emphasize that EPA must make decisions based on the information that is "available," and the courts have recognized that such a duty requires action on the basis of available information even if that information is imperfect. EPA cannot craft its systematic review process to incrementally exclude available information study-by-study, with the possibility of prohibiting use of the best available science simply because one or more of the underlying studies is imperfect in some manner. While certain systematic review approaches in exceptional cases may exclude from further consideration some studies because they entail a substantial risk of bias or have severe methodological shortcomings, EPA's proposed scoring approach appears to allow or require EPA to frequently exclude studies based solely on reporting flaws or other flaws that do not rise to the level of these exceptions.
As described more below, EPA's approach will also exclude certain reasonably available information on the basis that it does not meet EPA's preset expectations. For example, for monitoring data, environmental release data, completed exposure or risk assessments, and reports containing other exposure or release data, EPA plans to rate as "unacceptable" any data derived from occupational or non-occupational scenarios that do not precisely correspond to an occupational scenario EPA has identified within the scope of a given risk evaluation. Pp.75-76, 79-80, 86-87. The far more appropriate response to discovering reasonably available information revealing scenarios outside the scope of the risk evaluation would be for EPA to consider whether it needs to expand the scope of the risk evaluation and potentially the protocol (where any such changes would be clearly documented); nothing in TSCA authorizes or requires EPA to simply ignore that reasonably available information on the basis that it does not meet EPA's preset expectations.



54	EDF	1	Systematic Review	N/A
55	EDF	1	Systematic Review	N/A
56	EDF	1	Systematic Review	N/A

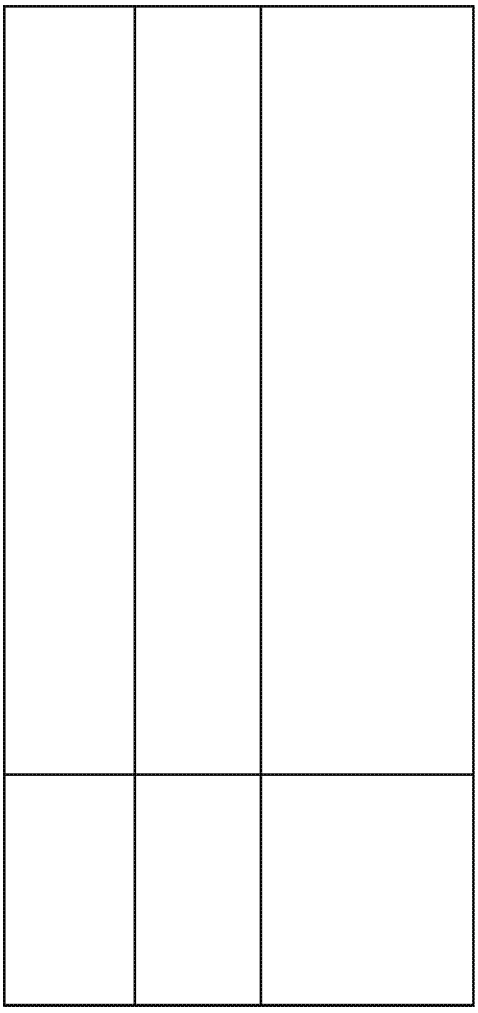
EPA's TSCA systematic review document is not representative of a true systematic review method as required by EPA's own risk evaluation rule, which requires inclusion of a "pre-established protocol" that addresses, among other things, how EPA will "integrate evidence". Born out of the clinical sciences, systematic review employs structured approaches to evidence identification, evaluation, and synthesis in a manner that promotes scientific rigor, consistency, transparency, objectivity, and reduction of bias. Indeed, systematic review transformed the field of medicine—serving today as the method for evaluating the effectiveness of interventions and diagnostic tools. Prominent systematic review methods and tools in medicine, particularly Cochrane and GRADE, have been shaped and refined over several decades based on empirical evidence and experience in application. Appropriately, leading systematic review approaches that have emerged in environmental health, including the UCSF Navigation Guide and the National Toxicology Program's literature-based reviews, have modeled themselves from these methods.
Bizarrely, EPA correctly cites authoritative sources on systematic review and at points describes processes that generally align with best practices, but then deviates substantially from those established best practices in detailing its specific plans for systematic review. Further, EPA provides no explanation or justification for its deviations.
OPPT's approach to systematic review lacks a generally linear progression, inconsistent with the conduct of true systematic review. In section three, Integration of Systematic Review Principles Into TSCA Risk Evaluation, EPA includes key excerpts from the preamble to the final rule Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act: "As defined by the Institute of Medicine, systematic review "is a scientific investigation that focuses on a specific question and uses explicit, pre-specified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies" (National Academy of Sciences, 2017). The goal of systematic review methods is to ensure that the review is complete, unbiased, reproducible, and transparent (Bilotta et al., 2014).****Key elements of systematic review include: a clearly stated set of objectives (defining the question); developing a protocol that describes the specific criteria and approaches that will be used throughout the process; applying the search strategy in a literature search; selecting the relevant papers using predefined criteria; assessing the quality of the studies using predefined criteria; analyzing and synthesizing the data using the predefined methodology; [and] interpreting the results and presenting a summary of findings. (p. 13-14)."



57	EDF	1	Systematic Review	p. 13-14
58	EDF	1	Systematic Review	N/A

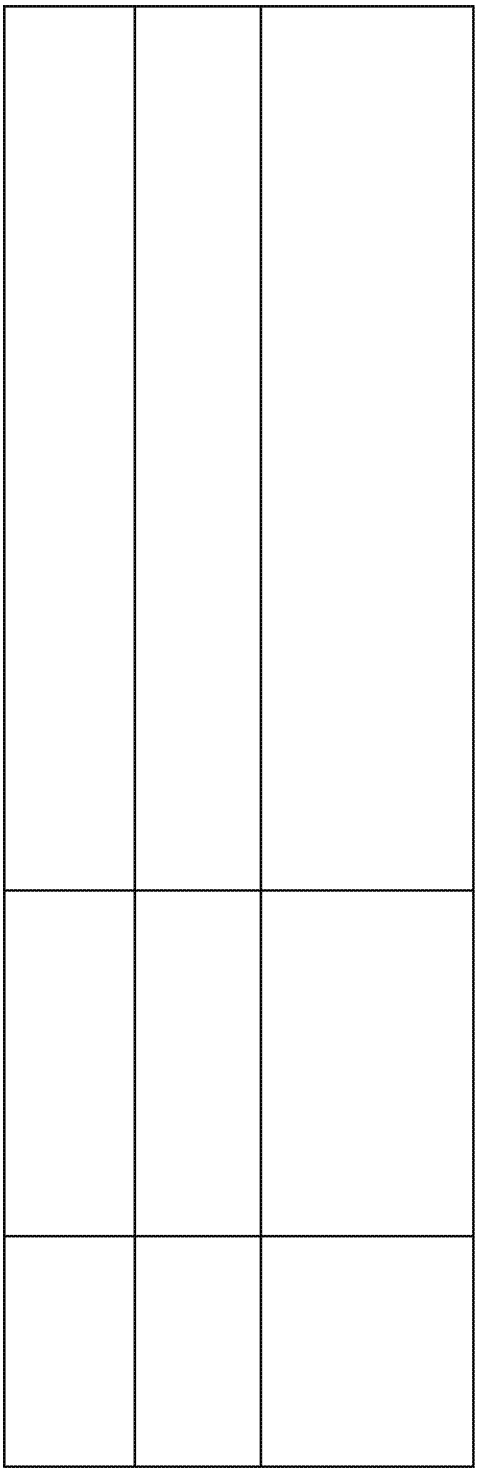
These excerpts (in comment 56) by and large reflect core tenets and approaches of a systematic review framework. However, the TSCA systematic review document makes evident that EPA has no interest in authentically applying systematic review. Indeed, it would be wrong to call what EPA has developed a systematic review framework, method, or tool. This becomes very evident in Figure 3-1 of the document, TSCA Systematic Review Process, copied below. The graphic portion of the figure illustrates a generally linear process in alignment with a true systematic review framework. However, an examination of the footnotes makes evident that the figure is a mirage:
-Footnote b: Data extraction may occur before or after data evaluation.
-Footnote c: Evaluation may occur during the scoping/problem formulation phase and/or during the analysis phase of the risk evaluation.
-Footnote d: Data relevancy issues are considered during the Data Screening, Data Evaluation and Data Integration phases.
-Footnote e: ***Most of the independent verification of the study results (i.e., study replicability) will be assessed during the Data Integration Step.
The effect of the footnotes is to undermine the basic premise and purpose of systematic review—to provide consistency, objectivity, transparency, and reduction of bias in the identification, evaluation, and integration of evidence, as foundationally supported by the development of a pre-defined protocol that articulates how these elements are to work. While it is difficult to parse out the specific meaning of EPA's footnotes, it is evident that the agency intends to jumble the process to such an extent that it is no longer a systematic review.

Also deeply concerning is EPA's use of "replicability" as a standard for independent verification. This is wholly inappropriate as it suggests that a study must be repeated in order to be considered valid or of high quality. A study's validity or quality is not dependent on whether the study and its findings have been repeated as discussed extensively in EDF's comments on EPA's proposal, Strengthening Transparency in Regulatory Science.20 EPA must strike this language in Figure 3-1 and anywhere else it may appear.



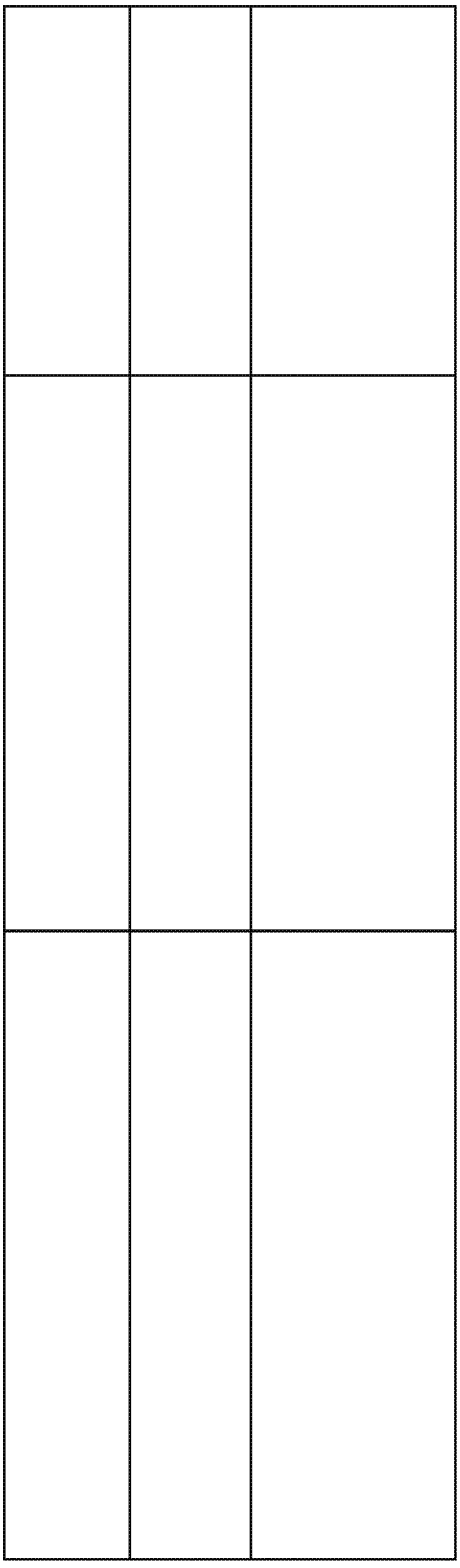
59	EDF	1	Systematic Review	p. 19
60	EDF	1	Systematic Review	p.19
61	EDF	1	Systematic Review	p.19

OPPT has failed to develop individual protocols for the first 10 chemicals undergoing risk evaluation. In the TSCA systematic review document, EPA states: "Protocol development is intended to pre-specify the criteria, approaches and/or methods for data collection, data evaluation and data integration. It is important to plan the systematic review approaches and methods in advance to reduce the risk of introducing bias into the risk evaluation process (p. 19, emphases added)". EPA has appropriately emphasized the importance of protocol development in systematic review –including its development at the outset. Authoritative sources on systematic review including Cochrane, National Academy of Sciences, the National Toxicology Program's Office of Health Assessment and Translation (OHAT), and the Navigation Guide all stress the import of upfront protocol development (excerpts from each document were included). Despite EPA's acknowledgement of the importance of upfront protocol development, EPA has failed to develop such protocols for the first 10 chemicals and it is not evident whether EPA plans to do so for future chemical risk evaluations. EPA states: "The first ten chemical substances were not subject to prioritization, the process through which EPA expects to collect and screen much of the relevant information about chemical substances that will be subject to the risk evaluation process. EPA has limited ability to develop a protocol document detailing the systematic review approaches and/or methods prior to the initiation of the risk evaluation process for the first ten chemical substances. For these reasons, the protocol development is staged in phases while conducting the assessment work. (p. 19)" EPA must develop upfront protocols for each chemical undergoing risk evaluation. The National Academy of Sciences in its recent review of the EPA Integrated Risk Information System (IRIS) program, Progress Toward Transforming the Integrated Risk Information System (IRIS) Program: A 2018 Evaluation, explained, "***[the] IRIS program is encouraged to complete the public-comment process and finalize the protocol before initiating the systematic review. Doing so will improve transparency in the IRIS process."
Insufficient time is not an acceptable justification for EPA's failure to develop protocols for the first chemicals undergoing risk evaluation. Upfront protocol development is a fundamental feature of systematic review, which EPA by regulation has explicitly included in its definition of the weight of the scientific evidence. Further, the challenges posed by the time constraints were magnified by EPA's illogical decision not to adopt state-of-the-art approaches to systematic review for chemical assessment that have been peer-reviewed, including by the National Academies, and applied and published (i.e., Navigation Guide, OHAT, and IRIS frameworks). Instead, OPPT has inexplicably chosen to develop de novo its own approach to systematic review, the result of which far from resembles a legitimate systematic review.
EPA must develop comprehensive protocols, make them publicly available, and subject them to public comment – prior to initiating subsequent steps of the risk evaluation process. For efficiency, we recommend that EPA simultaneously publish the protocols and chemical scoping documents. This would not be unlike the approach currently taken by the EPA IRIS program, which publishes its assessment plans (scoping and problem formulation) and protocols for public comment in advance of conducting toxicological reviews.



62	EDF	1	Systematic Review	p. 27
63	EDF	1	Systematic Review	p.27
64	EDF	1	Systematic Review	p. 14

OPPT has failed to describe its approach to evidence integration for the first 10 chemicals undergoing risk evaluation. EPA includes an evidence integration element in its systematic review approach (see Figure 3-1), but has failed to provide any substantive details on how it will execute this phase of the review, leaving a significant aspect of the risk evaluation processes a total black box. In the problem formulations for the first ten chemicals, EPA refers to the TSCA systematic review document for more details on how data integration will occur. But OPPT indicates in the TSCA systematic review document:"Data integration activities for the first ten TSCA risk evaluation [sic] are anticipated to occur after the TSCA Problem Formulation documents are released (Figure 1-1). EPA/OPPT will provide further details about the data integration strategy along with the publication of the draft TSCA risk evaluations. (p. 27, emphasis added)"
Beyond the fact that the public review process for the problem formulations did not have the benefit of knowing how EPA would conduct data integration, EPA's plan to describe and implement its approach to evidence integration simultaneously with the publication of the draft risk evaluations is problematic. Specifically, there is a high risk that EPA will inconsistently implement evidence integration across the first 10 chemicals undergoing risk evaluation as different groups of EPA staff concurrently conduct such evaluations absent a general reference methodology; as well as, significant risk for bias to be introduced in the implementation of evidence integration. It is antithetical to systematic review to concurrently develop and execute an entire step of the review process. More broadly, the absence of any description of how evidence integration will occur reflects EPA's general failure to develop, publish, and seek comment on upfront protocols for the chemicals undergoing risk evaluation. At the very least, EPA should immediately describe its general approach to evidence integration, referring to established systematic review approaches, including the OHAT, Navigation Guide, and IRIS methods. EPA should include this general approach in a revised TSCA systematic review document; and going forward, EPA should detail its specific approach to evidence integration in protocols developed for each chemical undergoing risk evaluation.
OPPT's approach to, and implementation of, systematic review should not provide for excessive iteration. In OPPT systematic review doucment, EPA states: "Although not shown in Figure 3-1, iteration is a natural component of systematic review and risk evaluation processes. There could be different reasons triggering iteration such as the failure of retrieving relevant data and information after the initial search and screening activities, which would require repeating the data collection stage of the systematic review process, or refinements to the initial search, screening and extraction strategies. (p. 14)" While adjustments during the conduct of a systematic review are acceptable, these adjustments should not be a frequent occurrence. The intent of systematic review is to create a structured, transparent, objective, and consistent approach to identifying, evaluating, and integrating evidence in a manner that reduces bias. Excessive iteration undermines this core purpose and provides a pathway for bias. Cochrane notes: "While the intention should be that a review will adhere to the published protocol, changes in a review protocol are sometimes necessary. *** While every effort should be made to adhere to a predetermined protocol, this is not always possible or appropriate. It is important, however, that changes in the protocol should not be made on the basis of how they affect the outcome of the research study. Post hoc decisions made when the impact on the results of the research is known, such as excluding selected studies from a systematic review, are highly susceptible to bias and should be avoided."



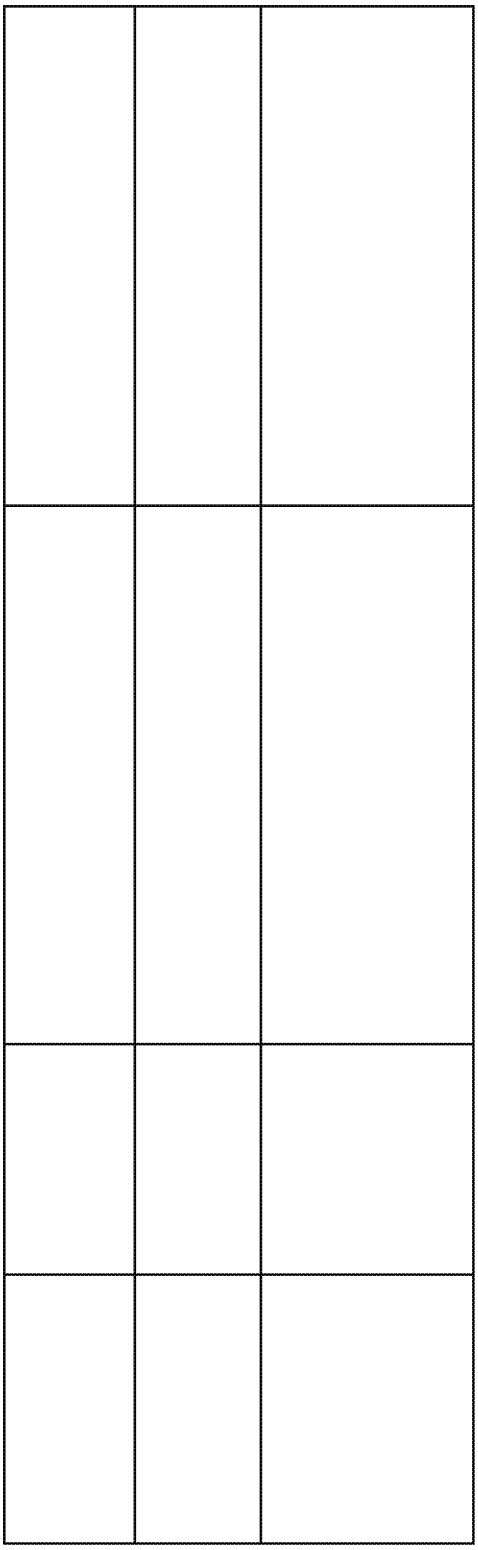
65	EDF	1	Systematic Review	p. 14
66	EDF	1	Systematic Review	P. 30
67	EDF	1	Systematic Review	P. 30
68	EDF	1	Systematic Review	p.33

This also exemplifies the problems that arise from EPA's failure to develop upfront protocols. Public comment on the upfront protocols would allow EPA to leverage the larger community in developing a rigorous protocol. A more rigorous protocol upfront would likely reduce the need for iteration. Additionally, in the absence of a protocol, it is impossible for the public to determine when and why EPA has modified its systematic review of a chemical. Documentation of changes to protocols is essential and EPA should provide public access to any changes in the protocol. Cochrane notes: "Changes in the protocol should be documented and reported in the 'Differences between protocol and review' section of the completed review, and sensitivity analyses (see Chapter 9, Section 9.7) exploring the impact of deviations from the protocol should be undertaken when possible." Cochrane systematic reviews are uploaded to PROSPERO, "an international prospective register of systematic reviews in health and social care" that creates a permanent record of protocols and allows changes to be tracked. As of 2013, all Cochrane protocols are automatically registered in PROSPERO. The UCSF Navigation Guide has registered several of its systematic reviews on chemicals in PROSPERO.

Use of scoring to evaluate individual study quality is wholly inappropriate and inconsistent with best practices in systematic review. As noted in the systematic review approach document, "EPA/OPPT developed a numerical scoring system to inform the characterization of the data/information sources during the data integration phase" (p. 30). Best practices in systematic review expressly discourage the use of scoring to rate individual studies. The Cochrane handbook for systematic reviews of interventions states: The use of scales for assessing quality or risk of bias is explicitly discouraged in Cochrane reviews. While the approach offers appealing simplicity, it is not supported by empirical evidence (Emerson 1990, Schulz 1995b). Calculating a summary score inevitably involves assigning 'weights' to different items in the scale, and it is difficult to justify the weights assigned. Furthermore, scales have been shown to be unreliable assessments of validity (Jüni 1999) and they are less likely to be transparent to users of the review. It is preferable to use simple approaches for assessing validity that can be fully reported (i.e. how each trial was rated on each criterion). (emphases added) [similar excepts from IOM and NAS follow]

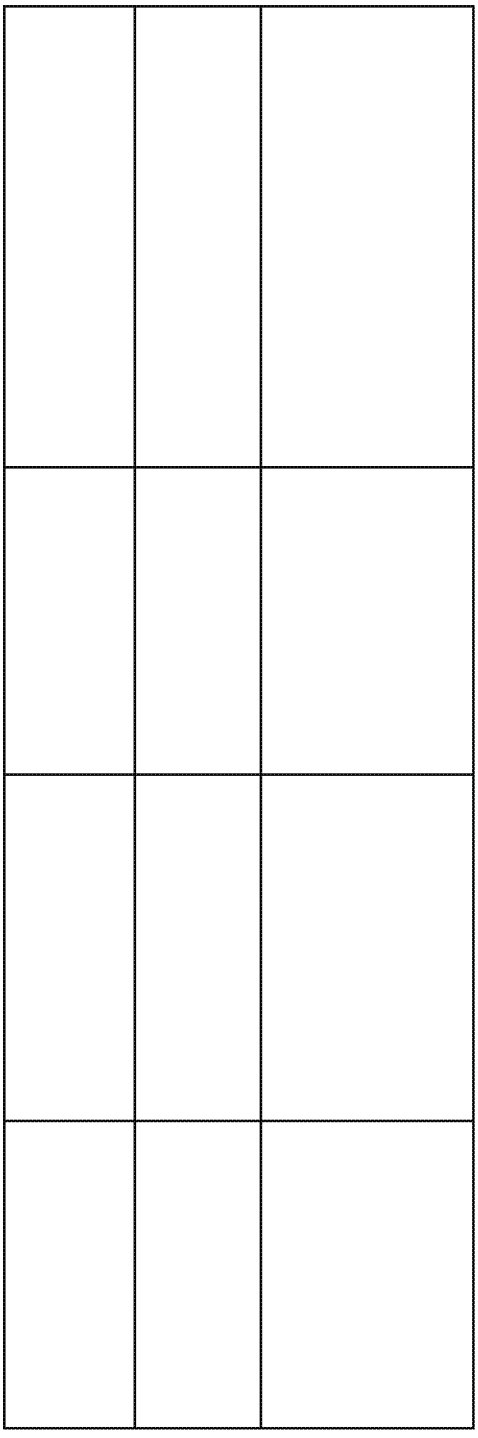
Despite these warnings [excerpts from Cochrane, IOM, IRIS] and explicit recommendations against applying scores and weights to study evaluation, OPPT has chosen to employ this strategy. Further, EPA has done this without providing any empirical evidence or scientific justification for why such a deviation from best practices in systematic review is reasonable, necessary, and valid. In reality, scientific justification for study scoring in a systematic review framework is scientifically unsound and does not exist.

The method by which EPA calculates a study's overall quality score highlights the arbitrary nature of the proposed scoring approach. [description of overall score cutoff] The choice of this particular cutoff structure is not science-based. Under this methodology, a study that scores 1.7 is equally weighted relative to a study that scores 2.3, despite the fact that the study with a score of 1.7 was only 0.1 away from being considered a High quality study, whereas the study scoring 2.3 was 0.1 from being considered Low quality. EPA's process amounts to nothing more than an algorithmic exercise lacking any empirical basis.



69	EDF	1	Systematic Review	N/A
70	EDF	1	Systematic Review	N/A
71	EDF	1	Systematic Review	N/A
72	EDF	1	Systematic Review	N/A
73	EDF	1	Systematic Review	N/A

In addition, collapsing all of a study's individual data quality metrics into a single overall study score presents significant challenges. For example, studies for which many criteria are not applicable can receive higher scores than studies that have more applicable criteria, even if they score the same in overlapping metrics. For instance, EPA gives an example on page 50 of a study within only one domain containing two metrics, "Verification or Plausibility of Results" and "QSAR Models," with weighted metric scores of 2 and 1, respectively, which contribute to an overall study score of 1.5. It is reasonable to assume that another study might also have weighted scores of 2 and 1 for the same two metrics, but in addition might have another separate metric that must be scored. If this additional metric has a weighted score of 2, then this second study will receive a lower score than the first study, despite the fact that they have identical scores on their shared metrics. This means that the presence of a third relevant metric is effectively discounting the scores of the other two metrics, despite the fact that the metrics are not related.
In applying a scoring methodology to study evaluation, EPA is not only deviating from best practices in systematic review, it is deviating from the strategies applied by sources that EPA used to develop this document including IRIS and OHAT. In line with best practices in systematic review, neither of these sources uses a numerical scoring approach to rate study quality. Thus, the very sources that EPA cites as resources used to develop its study evaluation approach explicitly state that they do not employ a scoring strategy and yet, EPA has chosen to develop a scoring methodology, without explanation or science-based justification. We strongly urge the agency to do away with a scoring approach to evaluating study quality.
OPPT's approach to weighting criteria is inconsistent with best practices in systematic review; lacks empirical evidence and justification; and is entirely arbitrary. As part of its scoring methodology, OPPT assigns greater weights to metrics that it deems more important than others. EPA refers to these as "critical metrics." However, in its 2014 review of the IRIS program, the NAS wrote that "there is no empirical basis for weighting the different criteria in the scores." OPPT's metric weights imply that the agency has some scientific basis for the degree to which a given metric criteria affects overall study quality. However, the reality is that there is no evidence to support this approach, while there is empirical evidence suggesting that quality scores and weighting lack validity, can be misleading, and introduce bias.
Disregarding best practices, OPPT provides vague, substantively empty explanations for why it has assigned greater weight to certain metrics. For example, in assigning weights to data quality metrics for occupational exposure and release data, OPPT states that "EPA used expert judgement to determine the importance of a particular metric relative to others," and that "EPA judged applicability and temporal representativeness to be the most important towards overall confidence, and these two metrics were determined to be twice as important as other metrics (weighting factors assigned a value of 2)." EPA's "explanation" amounts to arbitrary, subjective judgment and is particularly dubious because EPA has not interrogated its methodology in practice.
EPA states that "the weighting approach for some of the strategies may need to be adjusted as OPPT tests the evaluation method with different types of studies." This statement highlights the arbitrary nature of the weighting factors, and more broadly, the outright dismissal of basic tenets of systematic review. In effect, EPA is explicitly allowing a pathway for bias in its study evaluation approach, as the agency will be able to retrospectively favor some study metrics over others and adjust their weights as the results of the study evaluation process unfold—an approach that is antithetical to developing a science-based, systematic review framework.



74	EDF	1	Systematic Review	p.27, 34
75	EDF	1	Systematic Review	N/A
76	EDF	1	Systematic Review	p. 31

The TSCA systematic review document suggests problematic use of expert judgment. OPPT indicates that expert judgment will be applied throughout its systematic review process:"Professional judgment will be used at every step of the process and will be applied transparently, clearly documented, and to the extent possible, follow principles and procedures that are articulated prior to conducting the assessment (U.S. EPA, 2016)." While expert judgment is certainly part of systematic review, EPA's proposed application of expert judgment raises some concerns. Most notably, the document states that expert judgment may overrule the overall study score that has been developed through the systematic review process: "After the overall score is applied to determine an overall quality level, professional judgment may be used to adjust the quality level obtained by the weighted score calculation." (p. 34) OPPT states that "the reviewer must have a compelling reason to invoke the adjustment of the overall score and written justification must be provided," yet few details are given. For example, it is not clear what qualifies as a "compelling reason" to alter the quality score or whose professional judgment can overrule.

While we object to OPPT's use of a scoring methodology to evaluate studies, if there exist legitimate, science-based circumstances that merit changes to a study's "confidence level," they should be factored into the TSCA systematic review document and individual protocols to the extent possible. Further, EPA must, as it has indicated it will do, identify and provide written justification for any adjustment made to overall evaluations of study quality.

OPPT's TSCA Systematic Review document incorrectly and inappropriately conflates study reporting with study quality. In doing, EPA severely jeopardizes use of best available science and weight of the scientific evidence, as the effect of EPA's approach would be to score studies as "low quality" or even exclude studies on the basis of reporting deficiencies rather than actual study quality. Study reporting pertains to how well study authors describe various aspects of their research, including its design and findings. A well-reported study can be of poor quality and a high-quality study can be insufficiently reported. [explanation of risk of bias and quality] Best practices in systematic review strongly advise against conflating issues of reporting and other aspects of study quality when assessing individual studies. While there are some differences across leading systematic review approaches for chemical assessment with how to address reporting issues, its distinction and separation from study quality is clear. [excerpts from the OHAT Systematic Review Handbood, IRIS Draft chloroform assessment protocol, navigation guide, and STROBE statement]

In its TSCA Systematic Review document, OPPT acknowledges the need to delineate between reporting and study quality. "Reporting quality is an important aspect of a study that needs to be considered in the evaluation process. The challenge, in many cases, is to distinguish a deficit in reporting from a problem in the underlying methodological quality of the data/information source. (p. 31)" However, OPPT then chooses an approach that deviates from this established best practice. "The TSCA evaluation strategies incorporate reporting criteria within the existing domains rather than adding a separate reporting domain as recommended in some evaluation tools/frameworks." (p. 31)" OPPT supports this decision to evaluate these metrics in parallel by stating that the aim of its approach is to "assesses reporting and methodological quality simultaneously with the idea of untangling reporting from study conduct while the reviewer is assessing a particular metric for each domain." Even on its face, this explanation is incoherent: how does assessing the two qualities "simultaneously" lead to a reviewer "untangling" the two? This approach seems likely to achieve precisely the opposite of one of its stated goals.

77	EDF	1	Systematic Review	N/A
78	EDF	1	Systematic Review	N/A
79	EDF	1	Systematic Review	N/A
80	EDF	1	Systematic Review	NA
81	EDF	1	Systematic Review	p. 105
82	EDF	1	Systematic Review	N/A

EPA's decision to conflate reporting issues with study quality and comingle their consideration is significant: It could well lead the agency to not use the best available science and not apply a legitimate weight of the scientific evidence approach. For example, OPPT's scoring methodology contains, for each data quality evaluation domain, a set of "serious flaws" that cause a study to be excluded from further consideration in the review. The methodology includes instances in which reporting issues are considered fatal flaws. One of the fatal flaws for monitoring data from studies on consumer, general population and environmental exposure is that "geographic location is not reported, discussed, or referenced." (p. 99) This is inappropriate as relevant monitoring data may not be associated with a specific geographic location. For example, a consumer market survey that examines product-purchasing behaviors may be useful as proxy for estimating exposure even though it may not include location as a data field or may not publish location information in order to protect respondent privacy. The collected information could very well still be useful in ascertaining chemical exposures. Similarly, a study involving biomonitoring of children at several different childcare facilities would likely not specify the geographic location of the facilities for privacy reasons. Yet again, this information could be incredibly valuable in assessing exposure-response relationships.

Even more egregious is the profusion of reporting quality in metrics used to evaluate epidemiological studies. Insufficiencies in reporting by themselves will frequently result in data quality metric scores of low or even unacceptable. For example, absence of STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist items in epidemiological studies result in a metric score of unacceptable for metrics 2, 3, 4, 6, and 7, and a score of low in metric 15. A score of unacceptable in a single metric across any study quality domain will result in the exclusion of an entire study. This is wholly inconsistent with best practices in systematic review, departs from best available science, and would likely result in EPA not using reasonably available information. It also makes clear that EPA has not meaningfully, if at all, tested its systematic review approach, because if it had it would have found a number of high quality, epidemiological studies would be inappropriately excluded.

OPPT's TSCA systematic review document is fraught with problematic metric criteria that do not support the use of best available science. Limited time to comment has prevented an exhaustive review of all metric criteria, but below we highlight some of the problematic metric criteria identified thus far.

Lack of access to underlying study data will downgrade a study's score or eliminate it entirely from consideration. For some of OPPT's data quality metrics, a study must provide underlying data in order to receive a score of "High" or even be considered. Such a standard mirrors the extensive concerns raised by EPA's Strengthening Transparency in Regulatory Science proposed rule, a hugely problematic and widely criticized proposal. As with conflating reporting quality with study quality (see comment section 7), EPA erroneously conflates access to underlying data with study quality—a deeply misguided and misleading treatment of scientific evidence.

Example: For studies on consumer, general population, and environmental exposures to receive a score of "High" in Domain 3 (Accessibility/Clarity), Metric 8 (Reporting of Results), it must meet the following standard: "Supplementary or raw data (i.e., individual data points) are reported, allowing summary statistics to be calculated or reproduced." (p. 105) If the supplementary or raw data are not reported, a study's score is automatically downgraded, regardless of its quality.

Example: For a human epidemiological study to receive a score of "High" in Domain 4 (Potential confounding/variable control), Metric 14 (Reproducibility of analyses), it must meet the following standard: "The description of the analysis is sufficient to understand precisely what has been done and to be reproducible." If an epidemiological study does not meet this standard, EPA will give it a score of "Low."

83	EDF	1	Systematic Review	N/A
84	EDF	1	Systematic Review	p. 76
85	EDF	1	Systematic Review	p.76
86	EDF	1	Systematic Review	p. 77, 103, 110

EPA's invoking of "reproducibility" as a standard to receive a score of "High" in these metrics mirrors similar language in the EPA's censored science proposal, raising serious concerns about the extent to which EPA is effectively requiring that all underlying study data be made publicly available to be meaningfully considered. Also see comments in section 3.A regarding EPA's use of "replicability" as a "verification" standard. EDF incorporates by reference comments submitted by EDF on EPA's proposed rule, Strengthening Transparency in Regulatory Science.

The scoring system also makes clear that OPPT intends to exclude occupational exposure scenarios that are outside the scope of the risk evaluation. For occupational exposure and release data, Domain 2 (Representative), Metric 3 (Applicability) notes that the following will cause a study to be scored "Unacceptable": "The data are from an occupational or non-occupational scenario that does not apply to any occupational scenario within the scope of the risk evaluation." (p. 76)

When EPA discovers studies of occupational or non-occupational scenarios that EPA failed to identify at the scoping stage, EPA must consider whether it needs to revise its approach to the risk evaluation by broadening the scope. TSCA orders EPA to consider "available" and "reasonably available" information in crafting a risk evaluation, and if EPA discovers reasonably available information that reveals the existence of real-world occupational scenarios that EPA failed to identify earlier in the process, TSCA does not authorize EPA to simply ignore that information by labelling the information "unacceptable." Rather, the appropriate resolution is for EPA to consider whether EPA needs to expand the scope to address these real-world exposures. In most circumstances, those circumstances are now "known" to occur and EPA must analyze these known conditions of use.

OPPT's scoring scheme includes data quality metrics that are scored "low" when study data are more than a certain number of years old, but EPA has provided no evidence that older information is per se less informative. For example, it appears that EPA intends to give monitoring data studies a low ranking for the temporal representativeness metric if their data are more than 15 or 20 years old. See p.77, 103, 110. While EPA provides a cursory explanation that older information is allegedly less representative than more recent information, EPA has not provided any empirical evidence supporting this weighting scheme. The temporal representativeness metric that is applied to monitoring data from studies of occupational exposure and release highlights the arbitrary nature of OPPT's scoring approach. To receive a "High" confidence level for this metric, the data must have been collected "after the most recent permissible exposure limit (PEL) establishment or update or are generally, no more than 10 years old, whichever is shorter." (p. 77) To receive a "Medium" score, the data must meet the following requirement: "The monitoring data were collected after the most recent PEL establishment or update but are generally more than 10 years old. If no PEL is established, the data are more than 10 years but generally, no more than 20 years old." And finally, the metric is scored "Low" if the data "were collected before the most recent PEL establishment or update or are more than 20 years old if no PEL is established." There is no empirical basis for favoring data that is fewer than 10 years old more than data that is 20 years old, nor does OPPT even attempt to provide a justification for this distinction. This scoring criteria implies that 9 year-old data is just as valid as 2 year-old data, but is more valid than 11 year-old data. Furthermore, OPPT provides no clarification for how this metric will be applied. Will studies that are 10 years old at the time of the literature search be included in the systematic review, even if those studies are 11 years old during the data evaluation and data integration phases of the review? For longitudinal studies with multiple years' worth of data, will all of the data – or just the most recent year's data – need to fall within the stated time constraints of a given confidence level? These questions underscore the arbitrariness of the data quality criteria that OPPT's data evaluation strategy employs.

87	EDF	1	Systematic Review	p. 245
88	EDF	1	Systematic Review	p.35
89	EDF	1	Systematic Review	p.131

EPA inappropriately applies an adverse outcome pathway (AOP) standard to effect biomarkers in epidemiological studies. For epidemiological studies, Domain 6 (Other (if applicable) Considerations for Biomarker Selection and Measurement), Metric 17 (Effect biomarker (detection/measurement/information biases)) to receive a score of "High" an effect biomarker must be a "[b]ioindicator of a key event in an AOP." (p. 245) To receive a score of "Medium" "[b]iomarkers of effect [must be] shown to have a relationship to health outcomes using well validated methods, but the mechanisms of action is not understood." It is wholly inappropriate to downgrade a study involving biomarkers just because the adverse outcome pathway for an observed effect is unknown. For many chemicals, the biological processes underlying observed effects are not well understood or may not be understood at all. This is the case even for pharmaceuticals available on the market today. The National Research Council wrote in its 2014 report, Review of EPA's Integrated Risk Information System (IRIS) Process, that "if FDA were required to organize drug safety around mechanism, it would be nearly impossible to regulate many important drugs because the mechanism is often not understood, even for drugs that have been studied extensively."

The TSCA systematic review document risks discounting non-guideline studies. OPPT claims that its scoring methodology is not meant to systematically favor guideline studies over non-guideline studies. In some cases, reference to study guidelines (in addition to professional judgement) may be helpful in determining the adequacy or appropriateness of certain study designs or analytical methods. This should not be construed to imply that non-guideline studies necessarily have lower confidence than guideline studies. [p. 35] However, this statement is in itself contradictory. If OPPT is using study guidelines to determine the adequacy and appropriateness of study methods, then guideline studies are likely to receive the highest scores for these data quality metrics because that feature – adherence to a guideline – is used to define the criteria. On the other hand, non-guideline studies, which are more likely to deviate from these standards, will necessarily receive lower scores for these metrics.

Additionally, there are several instances in which the language of the data quality metrics suggests that guideline studies could consistently receive higher scores than non-guideline studies. For example, for experimental data derived from studies on consumer, general population, and environmental exposure (Appendix E), to receive a score of "High" in Domain 1 (Reliability), Metric 1 (Sampling Methodology and Conditions), a study must meet the following standard:

-Samples were collected according to publicly available SOPs, methods, protocols, or test guidelines that are scientifically sound and widely accepted from a source generally known to use sound methods and/or approaches such as EPA, NIST, ASTM, ISO, and ACGIH.

OR

-The sampling protocol used was not a publicly available SOP from a source generally known to use sound methods and/or approaches, but the sampling methodology is clear, appropriate (i.e., scientifically sound), and similar to widely accepted protocols for the chemical and media of interest. All pertinent sampling information is provided in the data source or companion source. (p. 131, emphasis added)

Thus, a study must either follow standard protocols or its methods must be similar to standard guidelines for the study to receive the highest score for this metric. This could systematically favor guideline studies over non-guideline studies.

90	EDF	1	Systematic Review	p. 215, 219
91	EDF	1	Systematic Review	p.33
92	EDF	1	Systematic Review	p.23, 24, 26

Similarly, the data evaluation criteria for in vitro toxicity studies (Appendix G) include language that suggests guideline studies would consistently receive higher scores than non-guideline studies. To receive a score of "High" in Domain 4 (Test Model), Metric 15 (Number per group), a study must satisfy the following requirement: "The number of organisms or tissues per study group and/or number of replicates per study group were reported and were appropriate for the study type and outcome analysis, and consistent with studies of the same or similar type." (p. 215, emphasis added) Here, "appropriate" directs the reader to current standards and guidelines developed by OECD, EPA, and FDA.52 On the other hand, a study would receive a score of "Medium" for this metric if it meets the following description:

-The number of organisms or tissues per study group and/or replicates per study group were reported but were lower than the typical number used in studies of the same or similar type (e.g., 3 replicates/strain of bacteria in bacterial reverse mutation assay), but were sufficient for analysis and unlikely to have a substantial impact on results. (p. 215, emphasis added)

Here, the basis for scoring a study as "Medium" rather than "High" is that the study did not use a standard methodology. However, to be scored a "Medium," that discrepancy cannot have affected the results significantly. This means that a study that does not use guideline methods is scored lower, despite the fact that the deviation from established methods has not affected the study's results. This would appear to systematically favor guideline studies over non-guideline studies. Similar language is found in Domain 7 (Data Presentation and Analysis), Metric 23 (Data interpretation). (p. 219)

One of the confidence levels that can be given to data quality metrics for any study type is "Not rated/applicable." This category includes instances in which "studies cite a literature source for their test methodology instead of providing detailed descriptions." (p. 33) Reviewers will only look at this cited literature source if the study under consideration "is not [otherwise] classified as 'unacceptable' during the initial review" based on an evaluation of all other data quality metrics. Given that many of OPPT's data quality metrics focus on reporting quality (which in itself is problematic, as discussed at length in comment section 7), it is reasonable to assume that a study could score "unacceptable" based on reporting issues when, in fact, the information of interest is detailed in another information source referenced by the study authors. Rather than using a "Not rated/applicable" placeholder when a study cites a literature source for its methodology, OPPT should seek out, integrate, and consider all reasonably available information as part of evaluating study quality.

OPPT notes that "one screener conducted the screening and categorization of titles and abstracts." (p. 24). This is inconsistent with best practices in systematic review, which recommend at least two individuals for all screening steps in order to minimize potential reviewer bias and ensure that all relevant data and studies are captured. As the IOM writes in its standards for systematic review in healthcare, "Without two screeners, SRs may miss relevant data that might affect conclusions about the effectiveness of an intervention. Edwards and colleagues (2002), for example, found that using two reviewers may reduce the likelihood that relevant studies are discarded." OPPT acknowledges the discrepancy between its approach and best practices in a footnote, stating that a lack of time and resources limited the office to one screener during the title/abstract screening step for the first ten chemicals. However, lack of time and/or resources is not a valid justification for failing to meet systematic review standards that empirically reduce risk of bias. Additionally, OPPT notes that the plan for future reviews is that, "Each article is generally screened by two independent reviewers using specialized web-based software." (p. 23, emphasis added) Similarly, for the data evaluation step OPPT states that, "Ideally, each data/information source will be screened by two reviewers, but one reviewer may be used." (p. 26). The use of two or more independent reviewers for each step of the screening process is not a standard that should be applied generally or only when OPPT can meet ideal targets, it is one that OPPT should adhere to without exception.

93	EDF	1	Systematic Review	N/A
94	EDF	1	Systematic Review	p.21
95	EDF	1	Systematic Review	N/A

Absent from the TSCA systematic review document is any consideration of the effect of financial conflict of interest on study results. Empirical evidence reveals that financial conflict of interest held by study authors or sponsors can influence study results. Leading systematic review organizations recognize and incorporate an evaluation of financial conflict of interest at some point in the systematic review process. [excerpt from Cochrane] Indeed, leading scientific journals increasingly require conflict-of-interest disclosures for manuscripts, recognizing the need to have such transparency. These increasingly required publication disclosures facilitate EPA's ability to collect and assess the potential impact conflicts of interest have on study results. EPA has chosen not to collect such information in its systematic review approach. While EDF opposes conflating reporting issues with study quality, it is worth noting the conspicuous omission from data quality metrics for epidemiological studies of STROBE checklist item #22, "Give the source of funding looking and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. At a minimum, we recommend EPA apply OHAT's approach to considering potential impacts of conflicts of interest on individual studies and the body of evidence. [excerpt from OHAT]
EPA makes a troubling, and potentially inaccurate, assertion about the CBI status of health and safety information in the TSCA systematic review document. the Data Collection section of the document EPA states: "EPA/OPPT also plans to search its internal databases for data and information submitted under TSCA (e.g., unpublished industry data). EPA will consider these data in the risk evaluations where relevant and whether or not they are claimed as confidential business information (CBI). If data/information are CBI, EPA/OPPT plans to use it in a manner that protects the confidentiality of the information from public disclosure." Under TSCA section 14(b)(2), health and safety studies and associated information are not eligible for protection from disclosure as CBI (subject to two narrow exceptions). 15 U.S.C. § 2613(b)(2). As with any other health and safety information, such information developed on chemicals to support the development of risk evaluations should be made publicly available. Health and safety information is not eligible under the law for CBI protection unless it would disclose process or mixture-portionality information. Also, EPA must generally scrutinize CBI claims to ensure that they are valid and substantiated per the requirements set out in TSCA section 14, and make its confidentiality determinations publicly available, see 15 U.S.C. § 2625(j)(1). The information referenced in the above quotes from the TSCA systematic review document clearly encompasses "health and safety studies" under TSCA's broad definition of that phrase, TSCA section 14(b)(2), as codified in EPA's regulations at 40 C.F.R. section 716.3. EPA must make this information public. See, e.g., 40 C.F.R. § 720.90(a) ("EPA will deny any claim of confidentiality with respect to information included in a health and safety study" except in limited circumstances).
OPPT must subject the TSCA systematic review document to peer review by established experts in the field given 1) the substantial digression from best practices in systematic review; 2) EPA's decision not to adopt leading systematic review approaches for chemical assessment that have been peer reviewed and developed in consultation with systematic review experts; and 3) the significant uncertainty associated with the outcome of applying its approach, including the implications for risk determination. OPPT must ensure its general approach to protocol development and data integration is included as part of such peer review.

96	UCSP PRHE	1	Systematic Review	N/A
97	UCSP PRHE	1	Systematic Review	N/A
98	UCSP PRHE	1	Systematic Review	N/A
99	UCSP PRHE	1	Systematic Review	N/A
100	UCSP PRHE	1	Systematic Review	N/A

EPA's systematic review framework under TSCA establishes EPA's "rules" for assembling and interpreting the scientific evidence on chemicals in commerce. These "rules" will determine, whether explicitly, implicitly, and/or by default, what evidence EPA will consider, and how it will evaluate that evidence when it is making decisions about potentially hazardous chemicals in commerce. Exposure to industrial, commercial, and consumer product chemicals is ubiquitous from the time of conception until death. As such, EPA's rules for gathering and interpreting the science that evaluates the relationship between these exposures and adverse health effects are of profound importance to the general public, and will have even greater impact on the potentially exposed or susceptible sub-populations Congress explicitly mandated EPA to protect: pregnant women, children, individuals with underlying health conditions, workers, and those with greater exposure and/or greater vulnerability to chemical toxicity and exposure. With so much at stake, we are deeply concerned by EPA's ad hoc and incomplete TSCA systematic review framework, which is inconsistent with current, established, best available empirical methods for systematic review. Moreover, as we detail below, the application of EPA's TSCA framework would likely result in the exclusion of quality research from EPA's decision-making. Accordingly, the TSCA systematic review method does not meet the mandate of the law to use the "best available science."

Based on the most current empirically demonstrated principles of systematic review methods, we provide EPA with concrete recommendations and approaches to correct its methodology and inform timely science-based decision-making to achieve the Agency's mission of protecting the public from harmful chemicals. [Summary comments are followed by detailed comments]

EPA's TSCA systematic review framework is ad hoc, incomplete, and does not follow established methods for systematic review that are based on the best available science.
We recommend: EPA should implement a systematic review method that is compatible with empirically based existing methods and aligns with the Institute of Medicine'se definition of a systematic review, including but not limited to, using explicit and pre-specified scientific methods for every step of the review. EPA should consider methods demonstrated for use in environmental health, and which have been endorsed and utilized by the National Academy of Sciences, i.e., the National Toxicology's Office of Heath Assessment and Translation systematic review method, and the Navigation Guide Systematic Review Method. EPA's TSCA systematic review framework should be peer-reviewed by qualified external experts in the field.

EPA's TSCA systematic review framework utilizes a quantitative scoring method that is incompatible with the best available science in fundamental ways:
a. Quantitative scores for assessing the quality of an individual study are arbitrary and not science-based; the Cochrane Collaboration and National Academy of Sciences recommend against such scoring methods.
b. EPA's scoring method wrongly conflates how well a study is reported with how well the underlying research was conducted; and
c. EPA's scoring method excludes research based on one single reporting or methodological limitation.
We recommend: EPA should not use a quantitative scoring method to assess quality in individual studies; it should not conflate study reporting with study quality; and it should not exclude otherwise quality research based on a single reporting or methodological limitation. Rather EPA should employ a scientifically valid method to assess risk of bias of individual studies.

EPA's TSCA systematic review framework does not consider financial conflicts of interest as a potential source of bias in research.
We recommend: EPA should assess study and author funding source as a risk of bias domain for individual studies.

101	UCSP PRHE	1	Systematic Review	N/A
102	UCSP PRHE	1	Systematic Review	N/A
103	UCSP PRHE	1	Systematic Review	N/A
104	UCSP PRHE	1	Systematic Review	p. 15
105	UCSP PRHE	1	Systematic Review	p. 15
106	UCSP PRHE	1	Systematic Review	N/A

The literature review step of EPA's TSCA systematic review framework incorporates select best practices, but also falls short of, or is unclear about, many other best practices for conducting a systematic and transparent literature review. We recommend: EPA should make its framework for conducting a literature review congruent with all of the Institute of Medicine's best practices and explicitly include rules for when the list of relevant studies will be considered final.
EPA's TSCA systematic review framework correctly recognizes that mechanistic data are not required for a hazard assessment, but EPA is not clear that these data, if available, can only be used to increase, and not to decrease, confidence in a body of evidence. We recommend: EPA should be explicit that mechanistic data can only be used to upgrade a hazard classification, or increase the confidence of a finding made based on evaluation of animal and human data, and that these data will not be used to decrease confidence in a body of evidence.
EPA's TSCA systematic review framework is not independent of the regulatory end user of the review. We recommend: EPA's TSCA systematic reviews should be produced independently of the regulatory end user of the review.
EPA's TSCA systematic review framework is ad hoc, incomplete, and does not follow established methods for systematic review that are based on the best available science. The best available scientific method for a systematic review (SR) specifies that all components of a review be established in a publically available protocol written prior to conducting the review to minimize bias and to ensure transparency in decision-making. For example, the Institute of Medicine defines a systematic review as a "scientific investigation that focuses on a specific question and uses explicit, prespecified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies" (emphasis added) (16)(p.1). A fatal flaw in EPA's SR framework is that it lacks essential SR elements, including but not limited to: (1) a protocol for executing a SR developed prior to conducting the SR; (2) an explicit method for evaluating the overall body of each evidence stream, i.e., animal, human, etc.; and (3) an explicit method for integrating two or more streams of evidence, including defined criteria for the type and level of evidence needed for a decision by EPA. Notably, EPA's TSCA SR Framework presents a diagram of a complete SR framework in Figure 3-1 (page 15) and states in footnote 4 on that page that the: Diagram depicts systematic review process to guide the first ten TSCA risk evaluations. It is anticipated that the same basic process will be used to guide future risk evaluations with some potential refinements reflecting efficiencies and other adjustments adopted as EPA/OPPT gains experience in implementing systematic review methods and/or approaches to support risk evaluations within statutory deadlines (e.g., aspects of protocol development would be better defined prior to starting scoping/problem formulation).
However, EPA's TSCA SR Framework then proceeds to describe an ad hoc and highly flawed method limited to only the data collection and, to a limited extent, the data evaluation components of a SR. Specifically, Figure S-1 below, excerpted from the National Academy of Sciences 2014 review of the EPA IRIS program's systematic review method (17), presents all of the components of a science-based SR. The red box indicates the parts of a SR method that EPA has included in its proposed framework. [Figure S-1 Systematic review in the context of the IRIS process is depicted with a red box around the Identify Evidence and Evaluate Studies]
EPA's piecemeal approach is not only in direct contradiction with the best available scientific methods for SR, but also incompatible with the regulatory definition off "weight of evidence" in the risk evaluation rule, which specifies a complete method spelled out in a protocol developed before conducting the review. Therefore, the TSCA systematic review method violates both TSCA statute and regulation.

107	UCSP PRHE	1	Systematic Review	p. 8, 9
108	UCSP PRHE	1	Systematic Review	p. 9

EPA explicitly states that it is proceeding with its first ten risk assessments in the absence of a pre-defined protocol and a complete method for systematic review. (p. 9) ... the purpose of the document is internal guidance that ... sets out general principles to guide EPA's application of systematic review in the risk evaluation process for the first ten chemicals ... EPA had limited ability to develop a protocol document detailing the systematic review approaches and/or methods prior to the initiation of the risk evaluation process for the first ten chemical substances. For these reasons, the protocol development is staged in phases while conducting the assessment work" (emphasis added). Additional details on the approach for the evidence synthesis and integration will be included with the publication of the draft TSCA risk evaluations." In effect, EPA is saying it does not have time to comply with its regulatory requirement to conduct a science-based systematic review, and will not actually develop its protocol until it completes the first ten systematic reviews. First, this approach is in clear violation with scientifically-validated approaches to conducting systematic reviews. In its review of the EPA's Integrated Risk Information System (IRIS) program's proposed SR methods, the National Academy of Sciences specified that, "Completing the literature search as part of protocol development is inconsistent with current best practices for systematic review, and the IRIS program is encouraged to complete the public-comment process and finalize the protocol before initiating the systematic review" (15)(Pg. 8). In the case of TSCA risk assessments, EPA is not only completing the literature search as part of protocol development, it is completing the entire systematic review in the absence of a protocol and complete method. It is blatantly biased to write the rules of evidence assembly and interpretation at the same time one is applying the rules, and as such, this method cannot be validly referred to as a science-based systematic review.

Second, a lack of time is not a credible rationale for EPA's failure to conduct a science-based systematic review for the first ten TSCA chemicals. There are multiple well-developed, science-based, peer-reviewed and validated methods for conducting systematic reviews in environmental health that EPA could readily apply, including the SR method and handbook developed by the Office of Health Assessment and Translation at the National Toxicology Program, and the Navigation Guide Systematic Review Method, which has been demonstrated in six case studies. The National Academy of Sciences cited both of these SR methods as exemplary of the type of methods EPA should use in hazard and risk assessment. Further, the National Academy of Sciences utilized both methods in its 2017 assessment of the potential health impacts of endocrine active environmental chemicals. Specifically, in its 2017 review the National Academy of Sciences found: "The two approaches [OHAT and Navigation Guide] are very similar ... and they are based on the same established methodology for the conduct of systematic review and evidence assessment (e.g., Cochrane Collaboration, AHRQ Evidence-based Practice Center Program, and GRADE). Both the OHAT and Navigation Guide methods include the key steps recommended by a previous National Academies committee (NRC 2014) for problem formulation, protocol development, specifying a study question, developing PECO statement, identifying and selecting the evidence, evaluating the evidence, and integrating the evidence" (19)(page 119)." Protocols developed for applying the Navigation Guide and the OHAT method have been published and can serve as a template to further expedite EPA's TSCA reviews.

109	UCSP PRHE	1	Systematic Review	p.26
110	UCSP PRHE	1	Systematic Review	p.35
111	UCSP PRHE	1	Systematic Review	N/A
112	UCSP PRHE	1	Systematic Review	N/A
113	UCSP PRHE	1	Systematic Review	p. 33, 225

Furthermore, the language of EPA's systematic review framework is confusing, contradictory, and poorly and incorrectly referenced with little science or policy foundation. This suggests the authors of EPA's TSCA Systematic Review Framework lack sufficient understanding of the scientific process integral to this work. A particularly egregious example is EPA's stated understanding of EPA's TSCA statutory science standards: "(Pg. 26) EPA/OPPT is required by TSCA to use the weight of the scientific evidence in TSCA risk evaluations. Application of weight of evidence analysis is an integrative and interpretive process that considers both data/information in favor (e.g., positive study) or against (e.g., negative study) a given hypothesis within the context of the assessment question(s) being evaluated in the risk evaluation." This directly contradicts EPA's own published rule which defines what a systematic review is (see footnote "e", above) and such an understanding completely subverts the purpose of a systematic review which is to explicitly avoid a simplistic analysis that would led to erroneous conclusions along the lines of stating that, for instance, "five studies are in favor (positive) and ten are against (negative) and therefore the weight is ... ".
Another bewildering statement by EPA concerns its highly quantitative scoring method, which is the main topic of its systematic review framework (see comment #2, below). EPA adds a caveat to the scoring method that says quantitative scoring is actually a qualitative method, and further: "The [scoring] system is not intended to imply precision and/or accuracy of the scoring results" (Pg. 35).
The ad hoc and incomplete nature of EPA's systematic review framework is incompatible in many additional fundamental ways, described further in detail below, with science based methods of systematic review developed, endorsed, and/or advanced by the: National Academy of Sciences; the Institute of Medicine; the National Toxicology Program; the Cochrane Collaboration; the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method; the international scientific collaboration that developed a framework for the "systematic review and integrated assessment" (SYRINA) of endocrine disrupting chemicals; the SYRCLE systematic review method for animal studies; the Campbell Collaboration's methods; and the Navigation Guide systematic review method developed by a collaboration of scientists led by the University of California San Francisco. Most of these organizations also pre-publish their protocols either online (i.e., the National Toxicology Program) or in PROSPERO (i.e., UCSF).
We recommend: EPA should implement a systematic review method that is compatible with empirically based existing methods and aligns with the Institute of Medicine's definition of a systematic review, including, but not limited to, using explicit and pre-specified scientific methods for every step of the review. EPA should consider methods demonstrated for use in environmental health, and which have been endorsed and utilized by the National Academy of Sciences, i.e., the National Toxicology's Office of Heath Assessment and Translation systematic review method, and the Navigation Guide Systematic Review Method. EPA's TSCA systematic review framework should be peer-reviewed by qualified external experts in the field.
Quantitative scores for assessing the quality of an individual study are arbitrary and not science-based. EPA's SR framework employs a quantitative scoring method to assess the quality of individual studies, assigning, based on its "professional judgment", various weights for quality domains and then summing up the quantitative scores to decide whether a study is of "high", "medium", or "low" quality [description of numberical scoring method and cut-off values] This overall scoring method is applied to all streams of evidence, and our comments reflect our objection to EPA's applying scoring to any and all streams of evidence. Illustrative of the scoring method, in Appendix H "Data Quality Criteria for Epidemiologic Studies," (page225) EPA presents how scoring is further applied to human studies, explaining: [description of critical metrics]

114	UCSP PRHE	1	Systematic Review	p.225
115	UCSP PRHE	1	Systematic Review	N/A
116	UCSP PRHE	1	Systematic Review	N/A

There is no scientific evidence to support EPA's selection of these "critical metrics" as being more important that other metrics, i.e., why within the "study participation" domain "selection" and "attrition" are more important than "comparison group"; and there are no data supporting EPA's choice of particular numbers for weighting these 'critical metrics' (i.e., some metrics are "twice" as important as the other metrics). Overall, there is no scientific justification for EPA to assign these or any other quantitative scoring measures for assessing the quality of an individual study. The implicit assumption in quantitative scoring methods is that we know empirically how much each risk of bias domain contributes to study quality, and that these domains are independent of each other. This is not a scientifically supportable underlying assumption. Research has documented that scoring methods have, at best, unknown validity, may contain invalid items, and that results of a quality score are not scientifically meaningful or predictive of the quality of studies. An examination of the application of quality scores in meta-analysis found that quality-score weighting produced biased effect estimates, with the authors explaining that quality is not a singular dimension that is additive, but that it is possibly non-additive and non-linear. Aggregating across quality criteria to produce a single score is recognized by preeminent systematic review methodologists as problematic and unreliable because the weights assigned are arbitrary and focus on the quality of reporting rather than the design and conduct of the research. Scoring is not utilized by empirically based systematic review methodologies, such as the Cochrane Collaboration or GRADE. As stated by the Institute of Medicine, "... systematic review teams have moved away from scoring systems to assess the quality of individual studies toward a focus on the components of quality and risk of bias".

The Cochrane Collaboration, founded in 1993, is an international non-profit and independent organization that produces and disseminates systematic reviews of healthcare interventions and is a key locus of the world's most authoritative expertise on systematic review methods. Cochrane's methodology states: "The current standard in evaluation of clinical research calls for reporting each component of the assessment tool separately and not calculating an overall numeric score (emphasis added)" The National Academy of Sciences in its review of the EPA's IRIS program's method for SR, strongly supported a methodology that did not incorporate quantitative scoring, stating "... Cochrane discourages using a numerical scale because calculating a score involves choosing a weighting for the subcomponents, and such scaling generally is nearly impossible to justify (Juni et al. 1999). Furthermore, a study might be well designed to eliminate bias, but because the study failed to report details in the publication under review, it will receive a low score. Most scoring systems mix criteria that assess risk of bias and reporting. However, there is no empirical basis for weighting the different criteria in the scores. Reliability and validity of the scores often are not measured. Furthermore, quality scores have been shown to be invalid for assessing risk of bias in clinical research (Juni et al. 1999). The current standard in evaluation of clinical research calls for reporting each component of the assessment tool separately and not calculating an overall numeric score (Higgins and Green 2008).

EPA's scoring method wrongly conflates how well a study is reported with how well the underlying research was conducted. Study reporting addresses how well research findings are written up, i.e., whether there is a complete and transparent description of what was planned, what was done, what was found, and what the results mean. Guidelines and checklists for authors have been developed to help ensure all information pertinent to assessing the quality and meaning of research is included in the report. The "Strengthening of Reporting of Observational Studies in Epidemiology" or "STROBE" Initiative is an example of a checklist of items that should be included in articles reporting such research.

117	UCSP PRHE	1	Systematic Review	p.31
118	UCSP PRHE	1	Systematic Review	N/A

EPA's SR Framework uses reporting measures in its scoring of the quality of human studies, including incorporating reporting guidelines into the reasons for scoring studies "low quality" (Metrics 1 and 15) or "unacceptable for use" (Metrics 2, 3, 4, 6, 7). EPA's SR Framework acknowledges that reporting is not the same as an underlying flaw in study methodology (Pg. 31), but then proceeds to ignore this distinction by using reporting as a measure of the quality of the underlying research. EPA's SR Framework not only does not "untangle" reporting from quality, it specifically conflates the two by using metrics in the STROBE reporting guidelines to score individual studies. The authors of the STROBE guidelines specifically note the guidelines are not a measure of the quality of the underlying research, stating: "The STROBE Statement is a checklist of items that should be addressed in articles reporting on the 3 main study designs of analytical epidemiology: cohort, case control, and cross-sectional studies. The intention is solely to provide guidance on how to report observational research well; these recommendations are not prescriptions for designing or conducting studies. Also, while clarity of reporting is a prerequisite to evaluation, the checklist is not an instrument to evaluate the quality of observational research (emphasis added). … Our intention is to explain how to report research well, not how research should be done. We offer a detailed explanation for each checklist item. Each explanation is preceded by an example of what we consider transparent reporting. This does not mean that the study from which the example was taken was uniformly well reported or well done; nor does it mean that its findings were reliable, in the sense that they were later confirmed by others: it only means that this particular item was well reported in that study."

The Cochrane Collaboration Handbook for conducting a SR clearly distinguishes reporting and bias, the latter which is defined as "a systematic error, or deviation from the truth, in results or inferences" (20). The Cochrane Manual for conducting systematic reviews is explicit about not conflating reporting with bias, stating: "Bias may be distinguished from quality. The phrase 'assessment of methodological quality' has been used extensively in the context of systematic review methods to refer to the critical appraisal of included studies. The term suggests an investigation of the extent to which study authors conducted their research to the highest possible standards. This Handbook draws a distinction between assessment of methodological quality and assessment of risk of bias, and recommends a focus on the latter. The reasons for this distinction include:

1. The key consideration in a Cochrane review is the extent to which results of included studies should be believed. Assessing risk of bias targets this question squarely.
2. A study may be performed to the highest possible standards yet still have an important risk of bias. For example, in many situations it is impractical or impossible to blind participants or study personnel to intervention group. It is inappropriately judgemental to describe all such studies as of 'low quality', but that does not mean they are free of bias resulting from knowledge of intervention status.
3. Some markers of quality in medical research, such as obtaining ethical approval, performing a sample size calculation and reporting a study in line with the CONSORT Statement (Moher 2001d), are unlikely to have direct implications for risk of bias.
4. An emphasis on risk of bias overcomes ambiguity between the quality of reporting and the quality of the underlying research (although does not overcome the problem of having to rely on reports to assess the underlying research)."

119	UCSP PRHE	1	Systematic Review	N/A
120	UCSP PRHE	1	Systematic Review	p.227
121	UCSP PRHE	1	Systematic Review	N/A

Importantly, in the application of EPA's SR Framework, studies can be scored as "low quality," and even excluded from EPA's review, based solely on a deficiency in reporting, irrespective of the quality of the underlying research. Research documents that important information is often missing or unclear in published research, as word limits, styles, and other specifications are highly variable, and non-standardized among peer-reviewed journals. As such, efforts to improve reporting are focused on uptake of reporting guidelines by journal editors and researchers. Improving reporting is needed in academic research, but as stated by the developers of the STROBE guidelines, "We want to provide guidance on how to report observational research well. … the checklist is not an instrument to evaluate the quality of observational research." Given the historical and present-day deficiencies in how studies are reported in the peer-reviewed literature, and because EPA's scoring system rates as 'unacceptable for use' any human study that does not report even one of five reporting metrics, EPA's proposal could reasonably be expected to lead to the exclusion from EPA's consideration much of the existing body of knowledge on the impact of environmental chemicals on human health, and is inconsistent with TSCA mandates to use the "best available science" and "reasonably available information." Applying flawed exclusion criteria that directly contradicts widely accepted empirically based SR methodological approaches will almost certainly result in flawed conclusions and threaten the protection of the public's health.
EPA's scoring method excludes research based on one single reporting or methodological limitation. In the "fatal flaw" component of EPA's SR Framework's scoring system, for each type of evidence stream, i.e., epidemiologic, animal, in vitro, etc., EPA created an arbitrary list of metrics that make studies "unacceptable for use in the hazard assessment," stating: EPA/OPPT plans to use data with an overall quality level of High, Medium, or Low confidence to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated as Unacceptable. Studies with any single metric scored as 4 will be automatically assigned an overall quality score of Unacceptable and further evaluation of the remaining metrics is not necessary (emphasis added). An Unacceptable score means that serious flaws are noted in the domain metric that consequently make the data unusable (or invalid)" (Pg. 227). There is no empirical basis for EPA's selected list of fatal flaws. Illustrative of this "fatal flaw" aspect of EPA' scoring system, for human epidemiologic studies (See Section H.5, Table H-8 (page 231), EPA lists six domains of study quality, i.e., study participation; exposure characterization; outcome assessment; potential confounding/variable control; analysis; and other considerations for biomarker selection and measurement, and 19 metrics to assess the six domains. A study that has even one of the 19 "serious flaws" metrics is considered to be "unacceptable for use."
EPA's list of "serious flaws" are not all equal indicators of study quality: For example, among human observational studies, any one of the list of 19 metrics can eliminate a study from consideration as EPA considers all of these "flaws" to be of equal import; as described in detail above, such weighting is arbitrary and not a science-based method.

122	UCSP PRHE	1	Systematic Review	p. 243
123	UCSP PRHE	1	Systematic Review	N/A
124	UCSP PRHE	1	Systematic Review	N/A
125	UCSP PRHE	1	Systematic Review	N/A

EPA's list of "serious flaws" are not all related to real flaws in the underlying research. Reporting guidelines are wrongly equated with "serious flaws" in study quality. Reporting guidelines are wrongly equated with "serious flaws" in study quality. For example, in scoring the quality of human studies, 5 of 19 "serious flaw" metrics (Table H-8) are STROBE reporting guidelines (STROBE checklist items # 6,7,8,13,15). A study would be scored as "unacceptable for use" by EPA based on any one of these STROBE reporting guidelines. As described above in comment #2a, the STROBE guideline developers explicitly state this is neither the intended nor a scientifically valid use of these guidelines. Analysis is equated with a "serious flaw" in study quality, but statistical power alone is not a valid measure of study quality. For example, EPA's framework excludes human studies that do not meet EPA's criteria for "high" in the analysis domain. EPA does not state how it will calculate whether a study is "adequately" powered. According to EPA's framework, to be included in an EPA review, a study must meet the "high" criteria in EPA's "Metric 13, Statistical power (sensitivity, reporting bias)" as presented in the box below. Studies that are not "high" quality for this metric would be designated as "unacceptable for use" by EPA: [excerpt from EPA Metric 13, Table H-9, p. 243]

First and foremost, EPA provides no method for how it will determine the "adequacy" of the statistical power of a study on which to base its score, and provides no rationale for excluding studies with less than 80% statistical power. According to STROBE guideline developers, … "before a study is conducted power calculations are made with many assumptions that once a study is underway may be upended; further, power calculations are most often not reported"

EPA's Metric 13 statistical power/sensitivity also appears to confuse bias with imprecision. Individual studies that are "underpowered" (for example, because in the real world the exposed population may not be large enough for statistical purposes even if they are health impacted) can still be potentially valuable to science-based decision-making. For example a small study may be imprecise but that should not be confused with whether it is biased (20); a small study can be imprecise but at the same time less biased than a larger study (17). Small "underpowered" studies can also be combined in a meta-analysis that increases the statistical power of the body of evidence to reflect the relationship between an exposure and a health impact. Additionally, "underpowered" studies that find a health effect to be present may be indicative of a larger effect size than anticipated. Thus, omitting such studies would severely bias the conclusions of the review.

Illustrative of how EPA's "analysis" metric could result in excluding high quality research that can inform science-based decision-making by EPA, in a 2017 systematic review by Lam et al. "Developmental PBDE Exposure and IQ/ADHD in Childhood: A Systematic Review and Meta-analysis," none of the 4 high-qualityp studies included in the meta-analysis reported a power calculation, and yet together, these studies found "a 10-fold increase (in other words, times 10) in PBDE exposure associated with a decrement of 3.70 IQ points (95% confidence interval:0.83,6.56)." It is also notable that one of the studies in the meta-analysis, Herbstman et al. 2010, was assessed by the review authors to be "probably high risk of bias" for "Incomplete Outcome Data." As such, this otherwise high quality study, i.e., all of the other domains were "definitely" or "probably" low risk of bias, would meet EPA's criteria for "unacceptable for use" based on STROBE reporting guideline #15, "Report numbers of outcome events or summary measures over time". In short, the Lam et al systematic review, using the best available scientific methods, found that a ubiquitous environmental contaminant is impacting human intelligence, a finding that was subsequently reviewed and endorsed by the National Academy of Sciences. Yet EPA's SR review framework would exclude crucial pieces of this body of evidence based on the Agency's inaccurate, non-science-based criteria for deeming studies 'unacceptable.' This is contrary to TSCA's mandate to use the best available science.

126	UCSP PRHE	1	Systematic Review	N/A
127	UCSP PRHE	1	Systematic Review	N/A
128	UCSP PRHE	1	Systematic Review	N/A

Level of exposure is equated with a "serious flaw". EPA's "exposure characterization" domain for human studies includes the level of exposure as a fatal flaw, stating: "For all study types: The levels of exposure are not sufficient or adequate (as defined above)
t to detect an effect of exposure (Cooper et al., 2016)." Unlike human experimental studies, which are largely precluded for ethical reasons, human observational studies can only be based on what exposures actually occur in the real world. EPA offers no explanation of how one could know whether the levels would be "sufficient or adequate" enough to detect an effect. Given the vagaries of this metric, it could be reasonably anticipated that it would permit EPA to arbitrarily exclude quality research from its decision-making.
We recommend: EPA should not use a quantitative scoring method to assess quality in individual studies; it should not conflate study reporting with study quality; and it should not exclude otherwise quality research based on a single reporting or methodological limitation. Rather EPA should employ a scientifically valid method to assess risk of bias of individual studies.

EPA's TSCA systematic review framework does not consider financial conflicts of interest as a potential source of bias in research. As observed by the Deputy Editor (West) of JAMA in 2010, "the biggest threat to [scientific] integrity [is] financial conflicts of interest". Yet EPA's systematic review framework is silent on how it will take into account this empirically documented influence on the results of scientific research. Underscoring this EPA SR framework deficiency is the fact that recent studies empirically document that industry sponsorship produces research that is favorable to the sponsor. The influence of financial ties on research can be traced to a variety of types of biases, and this conflict of interest needs to be distinguished from non-financial interests in the research, which can also affect research. The fact that funding source needs to be accounted for in some manner is empirically supported and not a subject of scientific debate; what scientists differ on is how to best address funding as a potential source of bias; for example, whether funding source is assessed as a specific risk of bias domain or considered at multiple points in the evaluation. For example, funding source is recommended as a factor to consider when evaluating risk of bias of individual studies for selective reporting, and then again for evaluating the body of evidence for publication bias, and/or to be considered as a potential factor to explain apparent inconsistency within a body of evidence. A 2017 Cochrane systematic review of industry sponsorship and research outcome concluded ... "industry sponsorship should be treated as bias-inducing and industry bias should be treated as a separate domain". The National Academy of Sciences in its review of the EPA IRIS program's SR method found that "Funding sources should be considered in the risk-of-bias assessment conducted for systematic reviews that are part of an IRIS assessment (p 79).

Notably, EPA's exclusion of consideration of funding source and other potential conflicts of interests is also internally inconsistent with EPA's own improper reliance on STROBE guidelines as quality measures: STROBE guidelines item #22 specified that "the source of funding and the role of funders, could be addressed in an appendix or in the methods section of the article". Importantly, including funding as a risk of bias as a domain does not mean excluding industry sponsored studies from EPA's hazard and risk assessment; it only means documenting funding as one of many domains of potential bias and evaluating its impact on the overall quality of the body of evidence.
We recommend: EPA should assess study and author funding source as a risk of bias domain for individual studies.

129	UCSP PRHE	1	Systematic Review	N/A
130	UCSP PRHE	1	Systematic Review	N/A
131	UCSP PRHE	1	Systematic Review	N/A

The literature review step of EPA's TSCA systematic review framework incorporates select best practices, but also falls short of, or is unclear about, many other best practices for conducting a systematic and transparent literature review. Overall, we commend the EPA for its efforts to incorporate many best practices for a comprehensive literature search in its systematic review framework. We compared EPA's framework for systematic review to the Institute of Medicine's (IOM's) best practices for the literature review step of a systematic review(See IOM 2011 Chapter 3. and TABLE E-1), which was applied by the National Academy of Sciences in its review of EPA's IRIS Program methods for systematic review (See Table 4-1 Pp. 43-55). We found EPA's framework to be consistent with 12 of IOM's 27 best practices for conducting a literature search (Figure 1 and Appendix 1). There are two key features of EPA's framework that are clearly inconsistent with IOM's best practices. EPA fails: (1) to include or exclude studies based on the protocol's pre-specified criteria, a practice that is critical to avoiding results-based decisions; and (2) to use two or more members of the review team, working independently, to screen and select studies, which is an essential quality-assurance measure. For the remaining 13 IOM best practices, EPA's framework is either unclearly stated (N=7) or the practice is not mentioned at all (N=6). However, based on the literature review methods presented in the First Ten TSCA Risk Evaluations, EPA's framework appears to have incorporated six additional best practices that are either unclear or not mentioned in EPA's SR framework: (1) work with a librarian or other information specialist trained in performing systematic reviews to plan the search strategy (IOM 3.1.1); (2) Design the search strategy to address each key research question (IOM 3.1.2); (3) Search regional bibliographic databases if other databases are unlikely to provide all relevant evidence (IOM 3.1.9); (4) Conduct a web search (IOM 3.2.5); and (5) Provide a line-by-line description of the search strategy, including the date of search for each database, web browser, etc. (IOM 3.4.1).
EPA should make its framework for conducting a literature review transparently congruent with all of IOM's best practices. This includes addressing two critical inconsistencies: (1) include or exclude studies based on the protocol's pre-specified criteria to prevent results-based decisions; and (2) Use two or more members of the review team, working independently, to screen and select studies, to ensure quality assurance. The transparency of the framework would be improved by specifying how EPA is addressing each best practice; at this juncture, how EPA intends to specifically handle many components of its literature searches could not readily be identified.
For example, the framework is unclear about whether EPA will include papers published in languages other than English. The exclusive reliance on English-language studies may lead to under-representation of the entire body of available evidence, and studies have also suggested that language bias might lead to erroneous conclusions. Furthermore, when considering the inclusion or update of an existing systematic review, studies have found that language-inclusive systematic reviews (including studies in languages other than English) were of the highest quality, compared with other types of reviews. Online translation tools are readily available to allow screeners to quickly evaluate study abstracts for relevance, and therefore we recommend EPA to incorporate non-English language studies in their screening and not simply exclude in advance these potentially relevant papers.

132	UCSP PRHE	1	Systematic Review	N/A
133	UCSP PRHE	1	Systematic Review	p.172
134	UCSP PRHE	1	Systematic Review	p.172
135	UCSP PRHE	1	Systematic Review	N/A

Additionally, EPA's framework should explicitly include rules for determining when the list of relevant studies will be considered final i.e., "stopping rules." Newer scientific studies will inevitably continue to appear in scientific journals and it will be impossible to continually attempt to include all these studies in a chemical assessment. To meet the deadlines as mandated by the Lautenberg Amendments, EPA should state clear stopping rules in the form of deadlines or criteria for when the body of included relevant studies will be finalized for the purposes of the chemicals assessment. We also strongly encourage EPA in its stated exploration of automation and machine learning tools, which can help speed the production of EPA's systematic reviews.
We recommend: EPA should make its framework for conducting a literature review congruent with all of the Institute of Medicine's best practices, and explicitly include rules for when the list of relevant studies will be considered final.

EPA's TSCA systematic review framework correctly recognizes that mechanistic data are not required for a hazard assessment, but EPA is not clear that these data, if available, can only be used to increase, and not to decrease, confidence in a body of evidence. EPA's TSCA framework (page 172) states that EPA will use the evaluation strategies for animal and in vitro toxicity data to assess the quality of mechanistic and pharmacokinetic data supporting the model, and may tailor its criteria further to evaluate new approach methodologies (NAMs). We agree with EPA that mechanistic data need to be evaluated in a manner comparable to how other streams of evidence are evaluated. Data generated by alternative test methods (such as high-throughput screening methods) are not different than any other type of in vitro or cell-based assay data that would be considered in a systematic review. These kinds of assays provide mechanistic data. However, in this case, as described in comment # 2 above, EPA's use of its evaluation strategies for animal and in vitro toxicity data would entail using a quantitative scoring method that is incompatible with the best available science in fundamental ways. EPA should employ a scientifically valid method to assess risk of bias of individual studies in all streams of evidence, including mechanistic data.

EPA's framework (page 172) states, "the availability of a fully elucidated mode of action (MOA) or adverse outcome pathway (AOP) is not required to conduct the human health hazard assessment for a given chemical (emphasis added)." We strongly agree with EPA that mechanistic data are not needed for a hazard assessment. In addition, EPA's framework should be explicit that mechanistic data are only used to increase confidence in a hazard assessment, and never to decrease confidence.

The National Academy of Sciences explicitly considered how mechanistic data could be utilized in a systematic review for evidence integration (19). The committee came to two conclusions. First, the same protocol for evaluating relevance and study quality must be used with mechanistic data as for any other study. For example, in the report's case study on phthalates, the committee was not able to integrate results from high-throughput assays because the cell lines used were of unknown relevance to the in vivo mechanism of phthalate toxicity (19)(pg.78). Second, the foundation of the hazard classification in a systematic review is the animal and human data, with the mechanistic data playing a supporting role. If mechanistic data is relevant, it can be used to upgrade a hazard classification, or increase the confidence of a finding made based on evaluation of animal and human data. A hazard classification is never made based on high-throughput or other kinds of mechanistic data alone(Pp. 158-9).
We recommend: EPA should be explicit that mechanistic data can only be used to upgrade a hazard classification, or increase the confidence of a finding made based on evaluation of animal and human data, and that these data will not be used to decrease confidence in a body of evidence.

136	UCSP PRHE	1	Systematic Review	N/A

EPA's TSCA systematic review framework is not independent of the regulatory end user of the review. EPA's TSCA systematic review/risk assessment process is not independent of the TSCA risk management process, a conflict that is incompatible with best scientific methods. EPA's SR framework was developed and is being implemented by the Office of Chemical Safety and Pollution Prevention (OCSPP), which is also responsible for regulating the environmental exposures under TSCA review. In contrast, other EPA chemical assessment programs such as the IRIS program are intentionally placed in a non-regulatory research arm (the Office of Research and Development), to create separation from the Agency's program office responsible for regulatory decisions. This separation supports IRIS's ability to develop impartial chemical toxicity information independent of its ultimate use by EPA's program and regional office in risk assessment and risk management decisions. The National Academy of Sciences supported this in its 2018 report, stating that: "Current best practices [for systematic reviews in other medical disciplines] recommended by the Institute of Medicine (IOM 2011) suggest that the IRIS teams involved in the systematic-review process should be independent of those involved in regulatory decision-making who use the products of the systematic-review teams (emphasis added)". This same principle should also be implemented across the Agency and specifically for TSCA assessments.

We recommend: EPA's systematic reviews should be produced independently of the regulatory end user of the review.

Problem Formulation Documents - Public Cor

1-BP SPECIFIC COMMENTS

#	Submitter	Attachments (#)	Category	Document Section #	Comment	RAD POC	Docket #
1							
2							

Action Needed

Problem Formulation Documents - Public Cor

1,4-DIOXANE SPECIFIC COMMENTS

#	Submitter	Attachments (#)	Category	Document Section #
1	APHA	1	Exposure	N/A
2	APHA	1	Exposure	N/A
3	APHA	1	Exposure	N/A

Comment	RAD POC	Docket #	Action Needed
For example, the agency relies on information from "several racing authorities" to conclude that dioxane is no longer used as a fuel additive in car racing. Even though the racing authorities "could not provide credible information on...whether [dioxane] is currently used at all," the agency nonetheless determined that "fuels and fuel additives" are not a condition of use for the purposes of the 1,4-dioxane risk evaluation and will be excluded.			
For example, even if domestic manufacture of 1,4-dioxane is included in the scope of the risk evaluation, inhalation of 1,4-dioxane in ambient air or ingestion of 1,4-dioxane in drinking water as a result of releases by domestic manufacturers will be excluded.			
For example, the agency said it intends to exclude exposure to 1,4-dioxane in drinking water because drinking water contaminants may be regulated under the Safe Drinking Water Act. (Notably, the agency does not regulate 1,4-dioxane under the Safe Drinking Water Act, nor has it proposed to do so.) EPA acknowledges that "[t]he general population may ingest 1,4-dioxane via contaminated drinking water." EPA reports that 341 water systems have measured 1,4-dioxane at concentrations associated with an excess cancer risk greater than or equal to one in one million. This level of risk "has often been considered a "benchmark" above which EPA has concerns for exposure to the general population" — that is,the agency has considered this level of risk to be unreasonable. Because EPA is excluding drinking water exposure to 1,4-dioxane from the risk evaluation, however, this unreasonable risk will be ignored.			

Problem Formulation Documents - Public Cor

PERC SPECIFIC COMMENTS

#	Submitter	Attachments (#)	Category	Document Section #	Comment	RAD POC	Docket #	Action Needed
1								
2								

Problem Formulation Documents - Public Cor

PV29 SPECIFIC COMMENTS

#	Submitter	Attachments (#)	Category	Document Section #	Comment	RAD POC	Docket #	Action Needed
1								
2								

Problem Formulation Documents - Public Comments

HBCD SPECIFIC COMMENTS

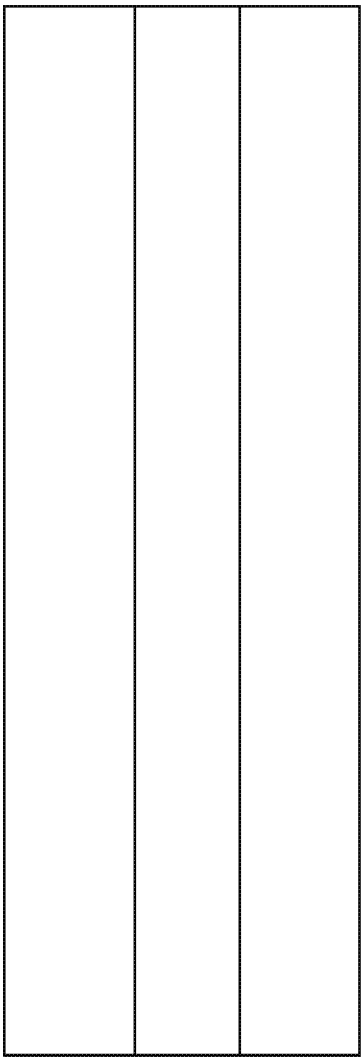
#	Submitter	Attachments (#)	Category	Document Section #
1	APHA	1	Exposure	N/A
2	APHA	1	Exposure	N/A
3	NTTC	1	PESS	N/A
4	NTTC	1	PESS	N/A

Comment
For example, EPA has concluded that "domestic manufacture of HBCD has ceased" based primarily on assurances provided by two recent manufacturers of the flame retardant. The agency does not indicate how it verified these assurances or how it will ensure that the purported cessation will continue in the future.
The agency has excluded domestic manufacture of expanded polystyrene (EPS) resin and extruded polystyrene (XPS) masterbatch from the HBCD evaluation based on reports by "all major North American manufacturers...of EPS resin" and comments by "major producers" of XPS masterbatch (emphasis added), respectively. These reports cover only manufacturers or producers that the agency considers "major." They cannot represent the activities of any other manufacturers of EPS resin or XPS masterbatch, including any future manufacturers.
A risk assessment based on the HBCD Problem Formulation will not be protective of tribal, rural, or urban subsistence populations as it fails to identify exposed subpopulations. Consequently, unless the Problem Formulation is changed to explicitly address these populations, the EPA Administrator will fail to carry out requirements as mandated by Congress in TSCA, as amended, June 22, 2016.
NTTC takes issue with the methodology used in identifying relevant literature for the scoping document. Arguably, the greatest change in TSCA is the mandate of health-based assessment and the inclusion of sensitive and exposed subpopulations in identifying the health risk of chemicals to the American people. Yet, while tribal based risk scenarios are readily available, they are not addressed in the Problem Formulation, and there is no evidence that an attempt was made to include them. Tribes are simply not mentioned, whether it be in the literature search or bibliography, the narrative, or conceptual model. The same holds for ethnic-urban subsistence and rural subpopulations.

RAD POC	Docket #	Action Needed

5	NTTC	1	PESS, Exposure	N/A

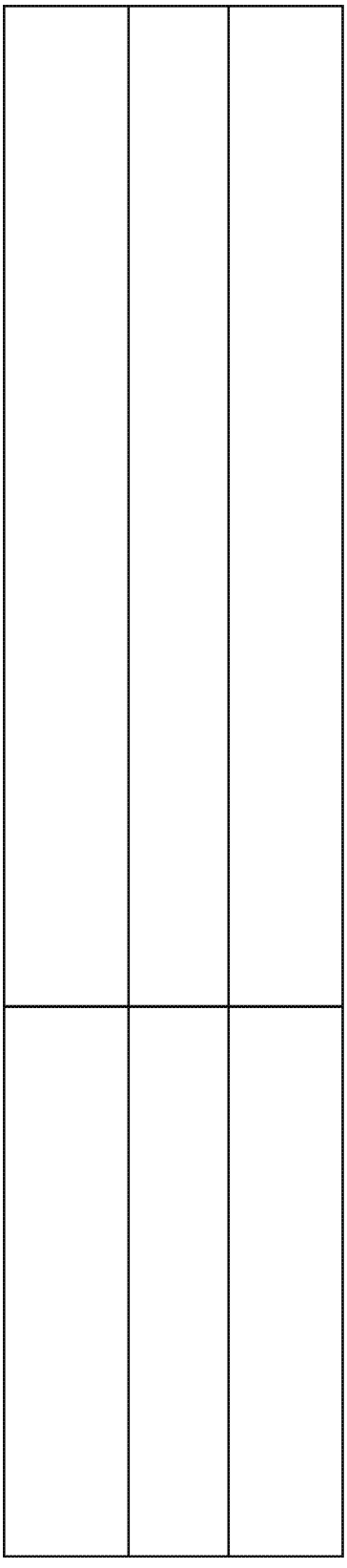
The EPA Office of Solid Waste is aware that permitted unlined municipal, and construction and demolition landfills are prevalent in Indian Country. The practice of open burning in burn barrels is widespread, and in Alaska Native villages the entire community wastestream is regularly burned without emissions control under a RCRA permit. Wild foods that the tribes depend on for their diet can be contaminated with HBCD via leachate and smoke, and whole communities can be exposed via inhalation and direct contact with wastes. Extruded and Expanded Polystyrene (XPS and EPS) insulation products are ubiquitous in Alaska and are used in ceilings, floors, interior walls, outside finished exterior walls, foundations and foundation wings, road beds, and more. The construction and demolition waste products, both residential and commercial, are brought to the unlined municipal landfills and dumpsites, or to unlined project-specific dumps. Nearly three-quarters of villages are within one mile of these disposal sites and their diets are dependent on locally hunted, fished, and gathered foods. Over eighty percent of these villages practice open burning, and because the sites are proximate, smoke from these disposal practices is commonly smelled by village residents. Even under the EPA's narrow Conditions of Use requirement, the resultant exposure scenarios for Alaska tribes, as well as Alaska rural residents that comprise more than half the population of the state, are left out. Many tribes are small communities with members being exposed in multiple ways. For example, the same worker who helped in the sawing of EPS board may be the landfill worker that carries the board to the dump and burns it, then goes home to their family where, now part of the community's "bystander" population, they have additional exposures by breathing the smoke, and consuming food and water that is contaminated from leachate.



6	NTTC	1	PESS	N/A
7	NTTC	1	PESS, Exposure	N/A

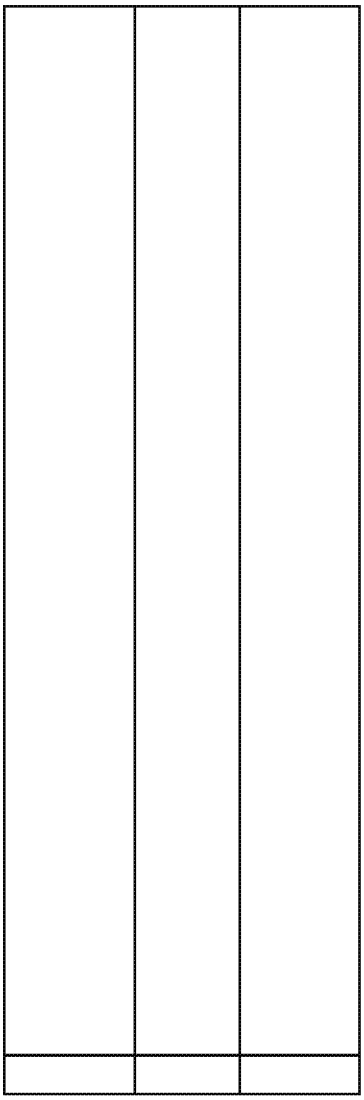
The following relevant language is excerpted from the Toxic Substances Control Act of 2016, as amended, pertaining to potentially exposed or susceptible subpopulation and to high-priority substances, and from the U.S. EPA Office of Chemical Safety and Pollution Prevention's May 2018 Problem Formulation for Cyclic Aliphatic Bromides Cluster (HBCD) respectively, with emphasis added relevant to the below comments.
The term "potentially exposed or susceptible subpopulation" means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly. The Administrator shall designate as a high-priority substance a chemical substance that
the Administrator concludes, without consideration of costs or other nonrisk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant by the Administrator. For HBCD, EPA considers workers, occupational non-users, consumers, and bystanders and certain other groups of individuals who may experience greater exposures than the general population due to proximity to conditions of use to be potentially exposed or susceptible subpopulations. EPA will evaluate whether groups of individuals within the general population may be exposed via pathways that are distinct from the general population due to unique characteristics (e.g., life stage, behaviors, activities, duration) that increase exposure, and whether groups of individuals have heightened susceptibility, and should therefore be considered potentially exposed or susceptible subpopulations for purposes of the risk evaluation.

Activity profiles are not representational. It is known that chlorinated and brominated flame retardants (BFRs) are being released into our environment throughout the world (Bi et al., 2007;35 Kakimoto, Akutsu, Konishi & Tanaka, 200836; Tue et al, 2010;37 Vázquez & Rizo, 2014). Studies such as these include finding brominated flame retardants (BFRs) in multiple biological samples in exposed humans including in the breast milk of mothers living at e-waste recycling sites in China and Vietnam. As noted below, similar practices of openly burning solid waste occur under approved exemption to federal law in Alaska tribal villages, and occur in and near other tribal communities where law enforcement is minimal and underfunded.



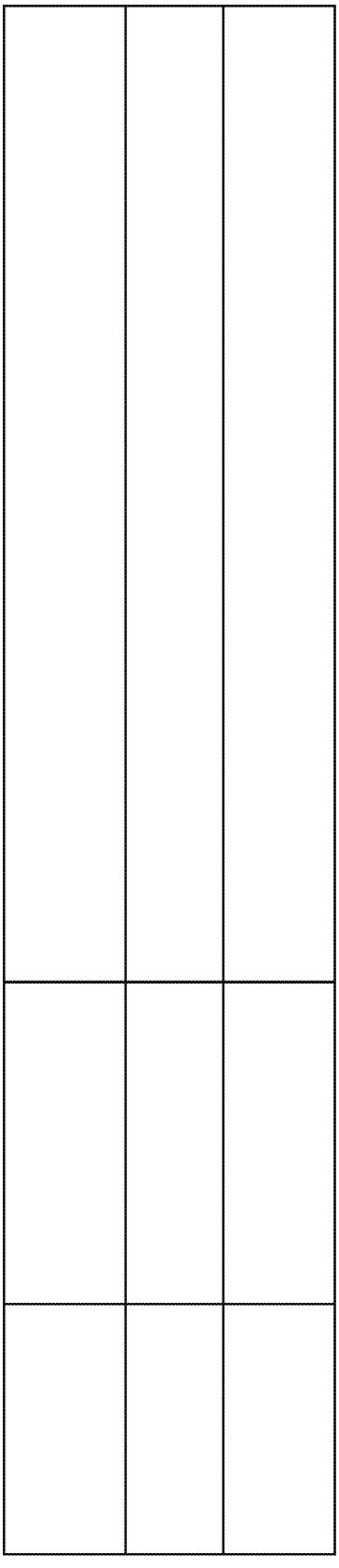
8	NTTC	1	PESS, Exposure	N/A
9				

Air Emissions from Open Waste Burning. This study investigated the occurrence of polychlorinated biphenyls (PCBs), and several additive brominated flame retardants (BFRs) in indoor dust and air from two Vietnamese informal e-waste recycling sites (EWRSs) and an urban site in order to assess the relevance of these media for human exposure (Tue et al. 2013). 50 The levels of PBDEs, HBCD, 1,2-bis-(2,4,6-tribromophenoxy)ethane (BTBPE) and decabromodiphenyl ethane (DBDPE) in settled house dust from the EWRSs (130-12,000, 5.4-400, 5.2-620 and 31-1400 ng g(-1), respectively) were significantly higher than in urban house dust but the levels of PCBs (4.8-320 ng g(-1)) were not higher. The levels of PCBs and PBDEs in air at e-waste recycling houses (1000-1800 and 620-720 pg m(-3), respectively), determined using passive sampling, were also higher compared with non-e-waste houses. The composition of BFRs in EWRS samples suggests the influence from high-temperature processes and occurrence of waste materials containing older BFR formulations. Results of daily intake estimation for e-waste recycling workers are in good agreement with the accumulation patterns previously observed in human milk and indicate that dust ingestion contributes a large portion of the PBDE intake (60%-88%), and air inhalation to the low-chlorinated PCB intake (>80% for triCBs) due to their high levels in dust and air, respectively.



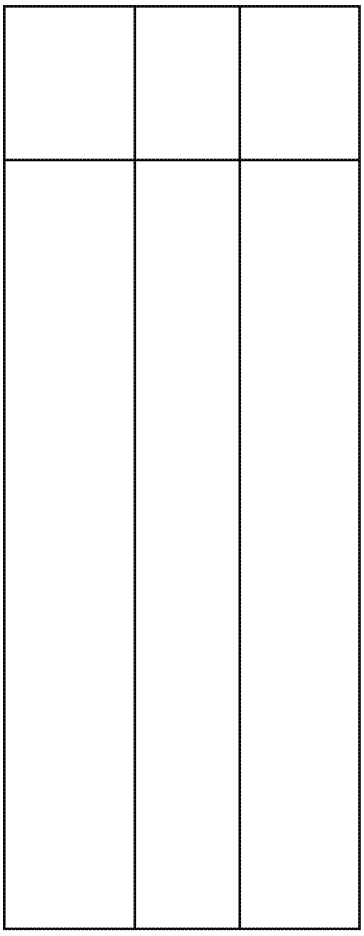
10	NTTC	1	General, Exposure	N/A
11	NTTC	1	General	N/A
12	NTTC	1	General, Exposure	N/A

Throughout Asia, non-PBDE BFRs like HBCD, have extensively polluted coastal waters (Isobe, Ogawa, Ramu, Sudaryanto, & Tanabe 2012). They used mussels as a bioindicator, as did studies by the US National Oceanic & Atmospheric Administration of coastal US waters (Isobe et al., 2012), Isobe et al were studying the presence of BFRs, the range throughout Asia, and the levels of concentrations. Among the three HBCD diastereoisomers, α-HBCD was the dominant isomer followed by γ- and β-HBCDs. Concentrations of HBCDs and DBDPE in mussels from Japan and Korea were higher compared to those from the other Asian countries, indicating extensive usage of these non-PBDE BFRs in Japan and Korea. Higher levels of HBCDs and DBDPE than PBDEs were detected in some mussel samples from Japan. The results suggest that environmental pollution by non-PBDE BFRs, especially HBCDs in Japan, is ubiquitous. This study provides baseline information on the contamination status of these non-PBDE BFRs in the coastal waters of Asia. More than 1,500 construction and demolition debris (CDD) landfills operate in the United States (U.S.), and U.S. federal regulations do not require containment features such as low-permeability liners and leachate collection systems for these facilities (Powell, Jain, Smith, Townsend, & Tolaymatl; 2015). Here we evaluate groundwater quality from samples collected in groundwater monitoring networks at 91 unlined, permitted CDD landfills in Florida, U.S. A total of 460,504 groundwater sample results were analyzed, with a median of 10 years of quarterly or semiannual monitoring data per site including more than 400 different chemical constituents. Downgradient concentrations of total dissolved solids, sulfate, chloride, iron, ammonia-nitrogen, and aluminum were greater than upgradient concentrations ($p < 0.05$). At downgradient wells where sulfate concentrations were greater than 150 mg/L (approximately 10% of the maximum dissolved sulfate concentration in water, which suggests the presence of leachate from the landfill), iron and arsenic were detected in 91% and 43% of samples, with median concentrations of 1,900 µg/L and 11 µg/L, respectively. These results show that although health-based standards can be exceeded at unlined CDD landfills, the magnitude of detected chemical concentrations is generally small and reflective of leached minerals from components (wood, concrete, and gypsum drywall) that comprise the bulk of discarded CDD by mass.
In August 2015, EPA published for public comment its TSCA Work Plan Chemical problem formulation and initial assessment documents for the three flame retardant clusters Brominated Bisphenol A (TBBPA), Chlorinated Phosphate Esters (CPE), and Cyclic Aliphatic Bromides (HBCD) (USEPA 2015c). In response NTTC provided written comments to that docket which we recapture here in relevance to problem formulation and risk evaluation under the amended TSCA.
NTTC appreciates EPA's inclusion of fish consumption by subsistence fishers and their children when evaluating exposure pathways for CPE. We specifically highlight EPA's commitment to account for the high-end fish consumption of subsistence fishers—including pregnant women, children and adults—the majority of whom are the tribal population.



13	NTTC	1	Human Health	N/A
14	NTTC	1	Human Health, Exposure	N/A

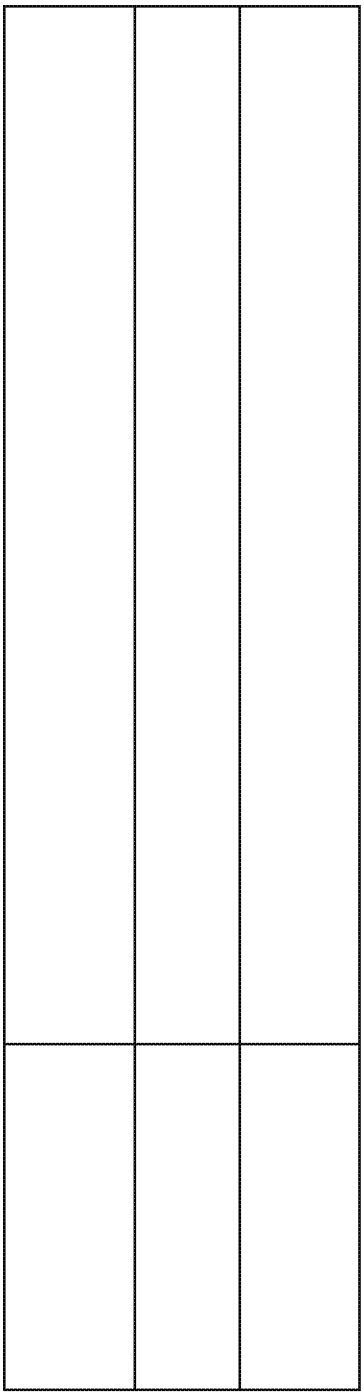
NTTC agrees with the need to evaluate the hazard endpoints that go beyond cancer risk and include target organ effects, reproductive and developmental effects, and neurotoxicity (U.S. EPA 2015d, p. 32, 34).
In CPE Problem Formulation of 2015, EPA stated it would exclude from further assessment the exposures of birds, terrestrial wildlife, or sediment-dwelling organisms as well as food other than fish. In our comments, NTTC noted its disagreement with EPA's decision as these exclusions fail to account for the subsistence diets of tribal populations, which include these species and other resources that consume these species. In the CPE Problem Formulation, EPA noted that [m]onitoring studies have reported the detection of TCEP in aquatic species, mammalian species, herring gull eggs and pine needles. ...these materials are likely bioavailable and could be observed in a biological matrix." (U.S. EPA 2015d, p. 22). The referenced studies showed detection of CPEs in the breast milk of women in Sweden, Asia, Japan, the Philippines, and Vietnam. These data demonstrate the need for consideration of the natural environment and food resources of tribal populations. Aquatic species, mammalian species and gull eggs are all natural resources upon which tribal populations subsist.



15	NTTC	1	Fate, Exposure	N/A
16	NTTC	1	PESS, Exposure	N/A

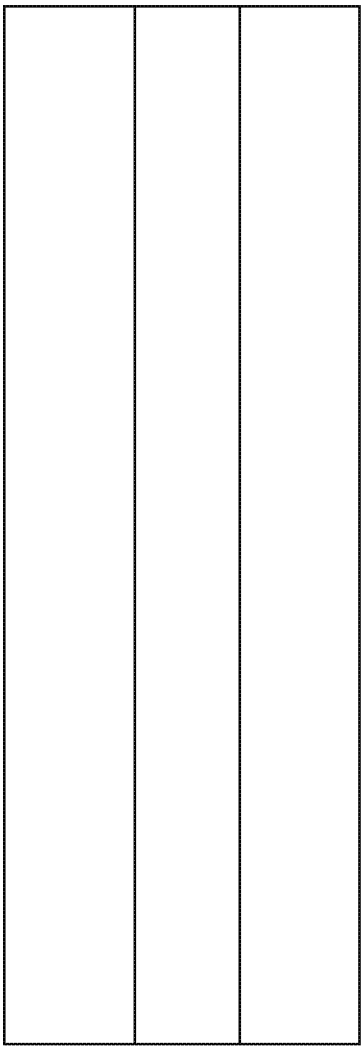
Yu et al. (2016) compiled and reviewed existing literature on the contamination status of BFRs in abiotic and biotic environments in China, including polybrominated diphenyl ethers (PBDEs), hexabromocyclododecane, tetrabromobisphenol A and new BFRs. 58 Temporal trends were also summarized and evaluated. Based on this review, it has been concluded that (1) high concentrations of PBDEs were generally related to the e-waste disposal processing, while the spatial distribution pattern of other BFRs was not necessarily in accordance with this; (2) extremely high concentrations of BFRs in indoor dust emphasized the importance of indoor contamination to human body burdens, while more work need to be done to confirm its contribution; (3) PBDEs in electronics dismantling workers were higher compared to the general population, indicating the occupational exposure should be of particular concern; (4) more data are now becoming available for BFRs in aquatic and terrestrial organisms not previously studied, while studies that consider the occurrence of BFRs in organisms of different trophic levels are still of urgent need for evaluating the fate of BFRs in the food web; and (5) limited data showed a decreasing trend for PBDEs, while more data on time trends of BFR contamination in various matrices and locations are still needed before the impact of regulation of BFRs can be assessed.

During problem formulation of HBCD, EPA identified inhalation, dermal and lifetime exposure assessments as data gaps that add uncertainty to EPA's risk assessment of HBCD. NTTC continues to maintain that EPA must include tribal populations in its plans to "conduct additional risk analysis on potential worker, general population, consumer and environmental exposures under the TSCA Existing Chemicals Program" (U.S. EPA, 2015e, p. 11).



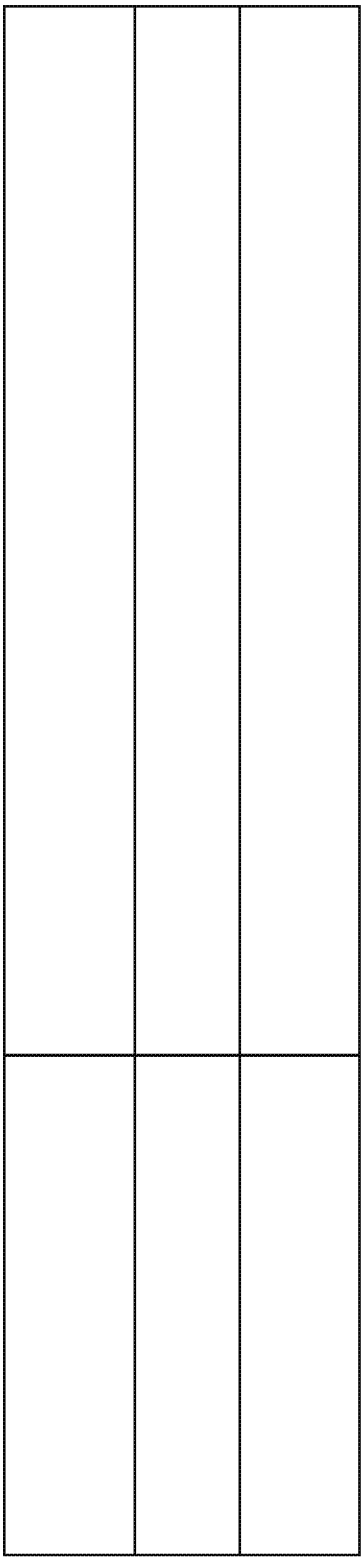
17	NTTC	1	PESS, Exposure	N/A

EPA noted that HBCD is a persistent pollutant in environmental media, expected to occur primarily as particulates, which may undergo long range transport, and is highly bioaccumulative with measured fish Bioconcentration factor values of greater than 18,000 (U.S. EPA, 2015e, p. 22). Given this, EPA must consider the impact of consumption by tribal citizens who live in geographic ranges where the majority of industrial-sourced particulates are deposited, who rely on traditional foods of fish and marine mammals which bioaccumulate toxins via fish and algae consumption. Further, on page 24 of the HBCD Problem Formulation, EPA referenced data of HBCD measured in the blubber and liver of various marine mammals; both of these tissues are a staple, consumed in large quantities, in Arctic tribal citizens' diets (U.S. EPA, 2015e, p. 76). Then, regarding bioaccumulation, EPA referenced studies that note the widespread detection and high levels of HBCD in aquatic and terrestrial organisms: invertebrates, fish, birds and their eggs, and marine mammals, all of which are traditional food resources of tribes. Finally, HBCD was detected in breast milk, adipose tissue, blood, and both maternal and umbilical serum (U.S. EPA, 2015e, p. 85). These references to EPA's own work highlights NTTC's principle that EPA must account for tribal populations, especially sensitive infant and child populations, in its risk evaluation of HBCD.



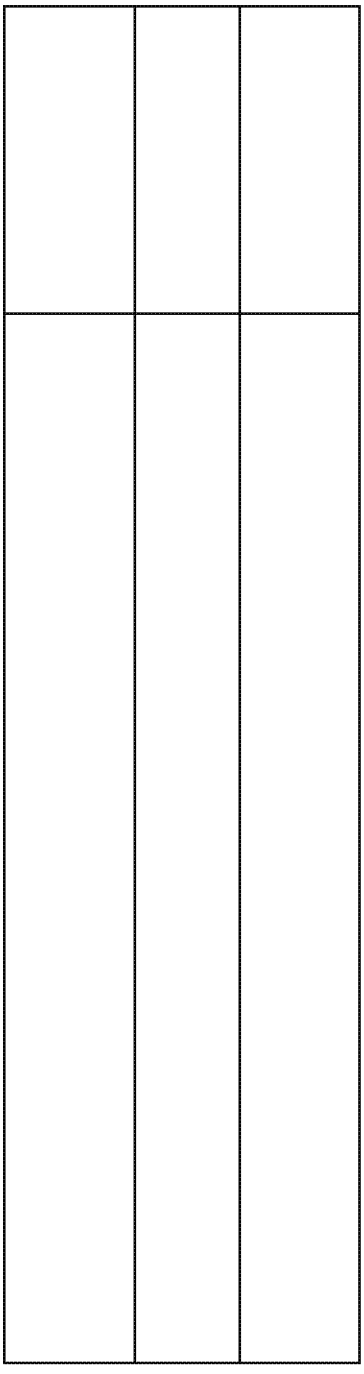
18	NTTC	1	PESS, Exposure	N/A
19	NTTC	1	Exposure	N/A

NTTC supports the EPA's decision for comprehensive studies for many endpoints for all cluster members of the TBB/TBPH cluster. NTTC also supports the EPA's statement of need for comprehensive studies on bioaccumulation of all brominated phthalate cluster (BPC) chemicals. Considering persistence and toxicity data on other brominated flame retardants, bioaccumulation and persistence data are extremely necessary. With the potential for acute and chronic toxicity, reproductive toxicity, and negative health effects on fetal development and endocrine disruption, it is alarming that the U.S. allows continued use of BPC chemicals. NTTC maintains its position that EPA must also consider chemical body burden, in addition to testing all cluster members individually and quantifying major degradation products. With suggested potential of long-term exposure of TBB/TBPH to wildlife, EPA stated that "chronic testing is recommended to address those organisms likely exposed in order to characterize potential population level effects"; and that suggested potential of "exposure and uptake by organisms present in water bodies including aquatic plants thus, hazard and bioaccumulation characterization is needed for these organisms" (U.S. EPA, 2015f, p. 39).60 (TBB/TBPH PF and DNA, 08/158, pp. 39) Therefore, NTTC reiterates that EPA must then also consider the effect of subsistence foods and traditional natural resources on the tribal population. This includes high-level consumption of marine mammals, such as whale, seal, walrus, and sea lion; fish and shellfish, such as salmon, herring, halibut, crab, and mussels; avian species such as duck, geese, and gull; and wildlife such as moose, deer, caribou, and elk.
Since the problem formulations noted above were released in 2015, NTTC has further researched these chemicals in commerce. Brominated flame retardants are found to be a frequent and at times high concentration of indoor dust in houses, apartments, daycare centers, and primary schools, and of the highest concentrations in North America and Europe (Malliari & Kalantzi, 2017). 61 "Results from the studies showed that dust ingestion was the dominant exposure pathway for most studied BFRs compared to indoor air inhalation and dermal contact, especially for infants and toddlers who have higher exposures than older children."



20	NTTC	1	Human Health	N/A
21	NTTC	1	Human Health, Exposure	N/A

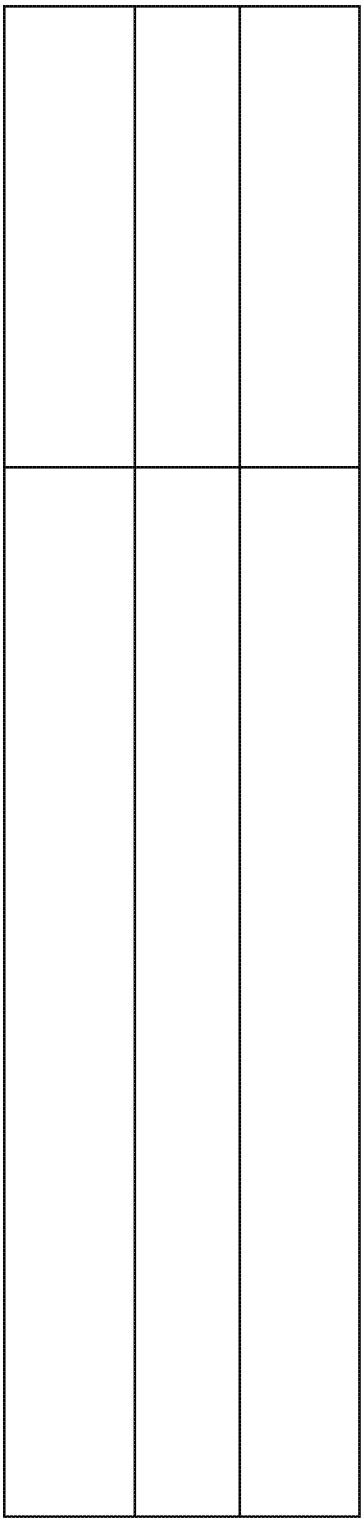
HBCD Toxicity testing has detected reproductive, developmental and behavioral effects in animals where exposures are sufficient (Marvin et al. 2011). Recent toxicological advances include a better mechanistic understanding of how HBCD can interfere with the hypothalamicpituitary-thyroid axis, affect normal development, and impact the central nervous system defects.
Fish represents source of nutrients and major dietary vehicle of lipophilic persistent contaminants (Maranghi 2013). The study compared the effects of two legacy and two emerging fish pollutants (Hexabromocyclododecane HBCD; 2,2',4,4'-Tetrabromodiphenyl ether BDE-47; 2,2',4,4',5,5'-Hexachlorobiphenyl PCB-153; 2,3,7,8-Tetrachlorodibenzo-p-doxin TCDD) in juvenile female mice exposed through a salmon based rodent diet for 28 days (dietary doses: HBCD 199 mg/kg bw/day; BDE-47 450 µg/kg bw/day; PCB-153 195 µg/kg bw/day; TCDD 90 ng/kg bw/day). Dose levels were comparable to previously reported developmental Lowest Observed Adverse Effect Levels. None of the treatments elicited signs of overt toxicity, but HBCD increased relative liver weight. All compounds caused changes in liver, thymus and thyroid; spleen was affected by BDE-47 and PCB-153; no effects were seen in uterus and adrenals. Strongest effects in thyroid follicles were elicited by PCB-153, in thymus and liver by BDE-47. HBCD and BDE-47 induced liver fatty changes, but appeared to be less potent in the other tissues. HBCD, BDE-47 and TCDD increased serum testosterone levels and the testosterone/estradiol ratio, suggesting a potential involvement of pathways related to sex steroid biosynthesis and/or metabolism. The results support the role of toxicological studies on juvenile rodents in the hazard characterization of chemicals, due to endocrine and/or immune effects.



22	NTTC	1	Fate, PESS, Exposure	N/A
23	NTTC	1	Fate, PESS, Exposure	N/A

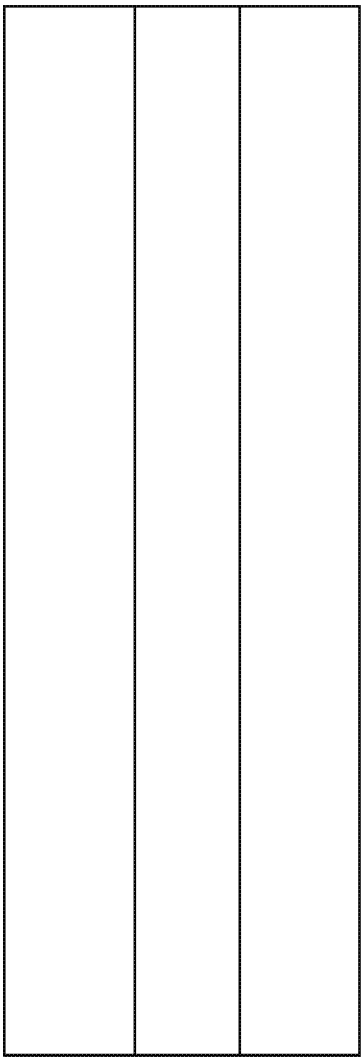
Extensive research indicates significantly concerning characteristics of brominated flame retardants (BFRs).
-BFRs are extensively present in environmental and biota samples worldwide,
-BFRs are persistent, bioaccumulative, and biomagnified, and
-BFRs have high potential toxicity to both ecological environment and human health.
Thus BFRs have an even greater potential toxicity to those who more frequently interact with and consume resources from the ecological environment. This is supported by Yu et al. (2016), Wang et al. (2010).

The particular relevance to tribal lifeways as representative of potentially exposed and susceptible subpopulations is especially demonstrated in Yu et al (2016) who, just two years ago, published their review of then existing literature on the contamination status of BFRs in abiotic and biotic environments in China, including polybrominated diphenyl ethers (PBDEs), HBCD, tetrabromobisphenol A (TBBPA), and newer brominated flame retardants (BFRs). Temporal trends were also summarized and evaluated. They concluded that (1) high concentrations of PBDEs were generally related to the e-waste disposal processing, while the spatial distribution pattern of other BFRs was not necessarily in accordance with this; (2) extremely high concentrations of BFRs in indoor dust emphasized the importance of indoor contamination to human body burdens, while more work need to be done to confirm its contribution;(3) PBDEs in electronics dismantling workers were higher compared to the general population, indicating the occupational exposure should be of particular concern; (4) more data are now becoming available for BFRs in aquatic and terrestrial organisms not previously studied, while studies that consider the occurrence of BFRs in organisms of different trophic levels are still of urgent need for evaluating the fate of BFRs in the food web; and (5) limited data showed a decreasing trend for PBDEs, while more data on time trends of BFR contamination in various matrices and locations are still needed before the impact of regulation of BFRs can be assessed.



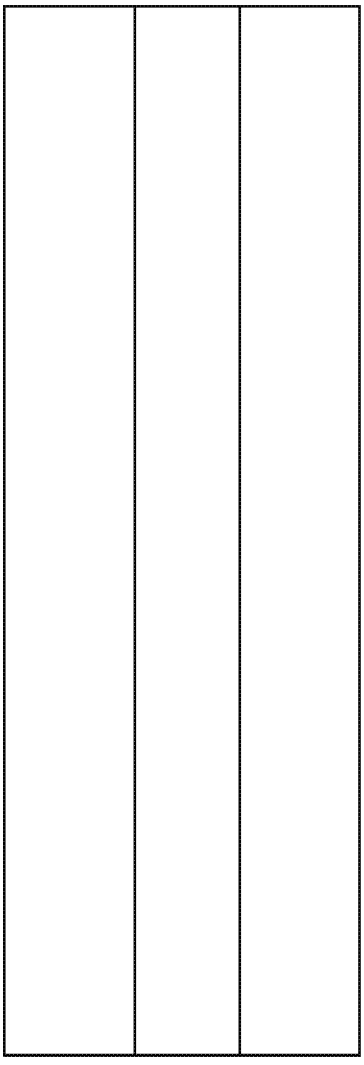
24	NTTC	1	Fate, PESS, Exposure	N/A

The findings by Wang et al. (2010) are alarming when considered in relation to tribal lifeways and the disposal of electronics in unlined landfills or dumpsites and by open burning. Brominated flame retardants (BFRs) in house dust from the electronic waste (ewaste) recycling and urban areas of South China showed that PBDE levels were comparable to the values found in North America. ...The distinct dust BFR profiles observed in the two studied areas were reflective of activities in these areas (electronics industry vs. e-waste recycling). The estimated daily intakes (EDIs) via house dust were much higher than those via other indoor pathways (air, fish, human milk, and toys). Despite the potentially low deleterious risk of PBDE exposure via house dust as suggested by the hazard quotients, this exposure pathway should be of great concern because of the higher BFR exposures for children and the presence of other BFRs (such as DBDPE) which have not yet been fully investigated. Housing-related exposures, for example. Used furniture and other items containing flame retardants, are gifted to others, purchased at thrift stores or yard sales, and found as free items on sidewalks, roadsides, and at the landfill. Furniture is kept longer than in urban and general populations, often well-passed typical time ranges and simply covered with sheets, blankets or other fabrics. Housing structures are older and smaller, similar to low-income and rural areas, and do not contain air conditioning systems, do not contain air filters, and residents rely on open windows and doors for summer cooling and for venting when cooking and cleaning. Dusting and vacuuming equipment is typically older, lesser quality, or non-existent. Inhalation and ingestion are major exposure pathways and EPA must account for these situations and factors when considering risk.



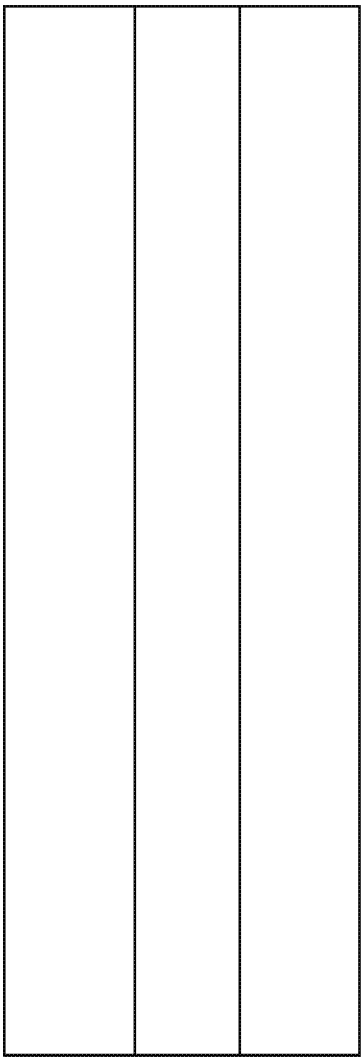
25	NTTC	1	Fate, PESS, Exposure	N/A

Public infrastructure: The tribal communities we discuss live with significantly outdated public infrastructure, e.g., private wells for drinking water, unplumbed homes, open dumping, kids playing around open dumps. They and others in rural America experience lifestyles much different from the urban centers: recreational swimming in natural water bodies, produce gardening and farming, living near open dumping, unpaved road dust, Arctic entry ways, living all or most of lifetime where they were raised, potlucks and social gatherings, sharing of harvested, grown, and gathered foods. For rural Alaska villages, drinking water, showers, and laundry are accessed at the public watering point, often called the washeteria, where wastewater is handled with only primary treatment. Schreder & La Guardia (2014) studied levels of flame retardants in residential house dust and laundry wastewater as a transport pathway from homes to the outdoor environment in communities near the Columbia River in Washington state (WA), accounting for influent and effluent from two wastewater treatment plants (WWTPs) servicing these communities. Of the 21 brominated and chlorinated compounds, including HBCD, detected in dust, 18 were also detected in laundry wastewater. Comparison of flame retardant levels in WWTP influents to estimates based on laundry wastewater levels indicated that laundry wastewater may be the primary source to these WWTPs.



26	NTTC	1	Fate, PESS, Exposure	N/A

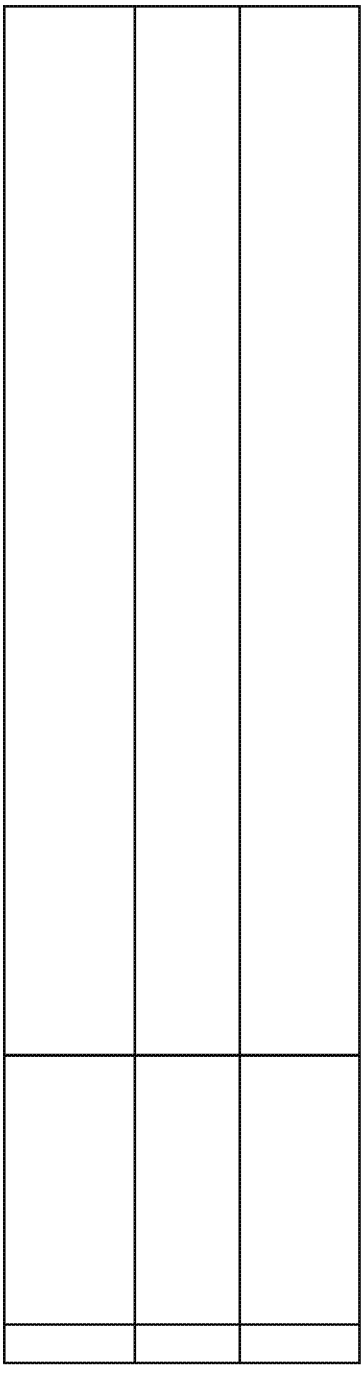
Lack of options in lifestyle. Food is gathered from land and waters locally and regionally. In the 2014 analysis update on subsistence in Alaska, rural residents harvested between 145 and 405 pounds per person per year of wild foods (Fall & Wolfe, 2016).67 The average per person per year amount was about 275 pounds for rural residents versus 19 for urban residents. That was about 0.75 pounds a day per person for rural residents versus 0.05 for urban residents. Costs of store items in Alaska villages and rural areas is prohibitive, often four or more times more expensive than in urban areas, so in general, there are less alternatives to food gathered. There are significantly fewer employment opportunities and higher costs for heating fuel, vehicle fuel, and household basic necessities due to added on cost of shipping items to village. Without incorporating these general profiles, the proposed problem formulations are not relevant to Tribal peoples, a susceptible subpopulation. La Guardia, Hale, Harvey, Mainor, Ciparis (2012) studied in-situ accumulation of HBCD, PBDEs, and several alternative flame-retardants in the bivalve and gastropod. While they found that several alternative brominated flameretardants (BFRs) were being detected in the environment, they noted that contaminant bioavailability is influenced by the organisms' ecology (i.e., route of uptake) and in situ environmental factors. We observed that the filter-feeding bivalve (Corbicula fluminea) and grazing gastropod (Elimia proxima), collected downstream from a textile manufacturing outfall. Maximum levels of total hexabromocyclododecane diastereomers (ΣHBCDs) and those of polybrominated diphenyl ethers (ΣPBDEs) were among the highest reported to date worldwide. While BDE-209 was once thought to be nonbioavailable and resistant to degradation, it was the dominant BFR present and likely debromination products were detected. Contributions of α- and β-HBCD were higher in tissues than sediments, consistent with γ-HBCD bioisomerization. Mollusk bioaccumulation factors were similar between HBCD and PBDEs with 4 to 6 bromines, but factors for TBB, TBPH, and BTBPE were lower. Despite different feeding strategies, the bivalves and gastropods exhibited similar BFR water and sediment accumulation factors.



27	NTTC	1	Fate, PESS, Exposure	N/A
28	NTTC	1	Fate, PESS, Exposure	N/A
29				
30				

In consideration of BFRs effect on flora, for example, Wu, Huang & Zhang (2016) investigation of the accumulation and phytotoxicity of technical hexabromocyclododecane (HBCD) in maize, using young seedlings exposed to solutions of technical HBCD at different concentrations. The results demonstrate HBCD accumulation in both the roots and shoots of the plant, HBCD causing DNA damage, and variances between HBCD diastereoisomers. The uptake kinetics showed that the HBCD concentration reached an apparent equilibrium within 96hr, and the accumulation was much higher in roots than in shoots. HBCD accumulation in maize had a positive linear correlation with the exposure concentration. The accumulation of different diastereoisomers followed the order γ-HBCD>β-HBCD>α-HBCD. Compared with their proportions in the technical HBCD exposure solution, the diastereoisomer contribution increased for β-HBCD and decreased for γ-HBCD in both maize roots and shoots with exposure time, whereas the contribution of α-HBCD increased in roots and decreased in shoots throughout the experimental period. These results suggest the diastereomer-specific accumulation and translocation of HBCD in maize. Inhibitory effects of HBCD on the early development of maize followed the order of germination rate>root biomass≥root elongation>shoot biomass≥shoot elongation. Hydroxyl radical (OH) and histone H2AX phosphorylation (γ-H2AX) were induced in maize by HBCD exposure, indicative of the generation of oxidative stress and DNA double-strand breaks in maize. An OH scavenger inhibited the expression of γ-H2AX foci in both maize roots and shoots, which suggests the involvement of OH generation in the HBCD-induced DNA damage. The results of this study will offer useful information for a more comprehensive assessment of the environmental behavior and toxicity of technical HBCD.

Several studies in the last few years have built on data analysis of BFRs in aquatic and terrestrial species. Sun et al. (2018) measured α-, β-, and γ-HBCDs in three freshwater fish—mud carp, tilapia, and plecostomus—from rivers and an electronic waste (ewaste) recycling site in Pearl River Delta, South China. [Summaries from mutliple studies]



Problem Formulation Documents - Public Cor

CCl4 SPECIFIC COMMENTS

#	Submitter	Attachments (#)	Category	Document Section #	Comment	RAD POC	Docket #	Action Needed
1								
2								

Problem Formulation Documents - Public Cor

NMP SPECIFIC COMMENTS

#	Submitter	Attachments (#)	Category	Document Section #	Comment	RAD POC	Docket #	Action Needed
1								
2								

Problem Formulation Documents - Public Comments

DCM SPECIFIC COMMENTS

#	Submitter	Attachments (#)	Category	Document Section #
1	APHA	1	Exposure, RegNex	N/A
2				

Comment	RAD POC	Docket #	Action Needed
For example, EPA intends to exclude inhalation of methylene chloride in ambient air. The agency claims that, because methylene chloride is listed as a hazardous air pollutant under the Clean Air Act, this pathway is "adequately assess[ed] and effectively manage[d]" under another statute and need not be considered under TSCA. This is incorrect. EPA manages hazardous air pollutants by requiring source categories to reduce emissions based on what is achievable using certain technologies. The agency does not require source categories to eliminate all emissions, and the remaining emissions can present significant risks. In the case of methylene chloride in ambient air, there is no reason to believe that exposure and risk are effectively managed. As the agency acknowledges, "levels of methylene chloride in the ambient air are widespread and shown to be increasing."			

Problem Formulation Documents - Public Cor

TCE SPECIFIC COMMENTS

#	Submitter	Attachments (#)	Category	Document Section #	Comment	RAD POC	Docket #	Action Needed
1								
2								

Problem Formulation Documents - Public Cor

ASBESTOS SPECIFIC COMMENTS

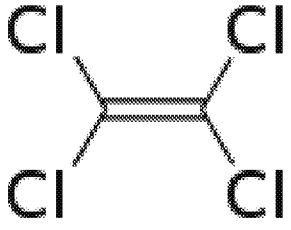
#	Submitter	Attachments (#)	Category	Document Section #	Comment	RAD POC	Docket #	Action Needed
1								
2								

EPA Document# EPA-740-R1-7017
May 2018
Office of Chemical Safety and
Pollution Prevention

States
Environmental Protection Agency

Problem Formulation of the Risk Evaluation for Perchloroethylene (Ethene, 1,1,2,2-Tetrachloro)

CASRN: 127-18-4



May 2018

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ACKNOWLEDGEMENTS
This report was developed by the United States Environmental Protection Agency (U.S. EPA), Office of Chemical Safety and Pollution Prevention (OCSPP), Office of Pollution Prevention and Toxics (OPPT).

Acknowledgements
The OPPT Assessment Team gratefully acknowledges participation and/or input from Intra-agency reviewers that included multiple offices within EPA, Inter-agency reviewers that included multiple Federal agencies, and assistance from EPA contractors GDIT (Contract No. CIO-SP3, HHSN316201200013W), ERG (Contract No. EP-W-12-006), Versar (Contract No. EP-W-17-006), ICF (Contract No. EPC14001) and SRC (Contract No. EP-W-12-003).

Docket
Supporting information can be found in public docket: EPA-HQ-OPPT-2016-0732

Disclaimer
Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation or favoring by the United States Government.

ABBREVIATIONS

°C	Degrees Celsius
1-BP	1-Bromopropane
ACGIH	American Conference of Government Industrial Hygienists
AEGL	Acute Exposure Guideline Level
ATSDR	Agency for Toxic Substances and Disease Registries
atm	Atmosphere(s)
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
CAA	Clean Air Act
CASRN	Chemical Abstracts Service Registry Number
CBI	Confidential Business Information
CCL_4	Carbon Tetrachloride
CDC	Centers for Disease Control
CDR	Chemical Data Reporting
CEHD	Chemical Exposure Health Data
CEPA	Canadian List of Toxic Substances
CERCLA	Comprehensive Environmental Response, Compensation and Liability Act
CFC	Chlorofluorocarbon
CHIRP	Chemical Risk Information Platform
cm^3	Cubic Centimeter(s)
COC	Concentration of Concern
CoRAP	Community Rolling Action Plan
cP	Centipoise
CPCat	Chemical and Product Categories
CPSC	Consumer Product Safety Commission
CSCL	Chemical Substances Control Law
CWA	Clean Water Act
DNAPL	Dense Non-Aqueous Phase Liquid
ECHA	European Chemicals Agency
EDC	Ethylene Dichloride
EG	Effluent Guidelines
EPA	Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act
ESD	Emission Scenario Documents
EU	European Union
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug and Cosmetic Act
FHSA	Federal Hazardous Substance Act
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
g	Gram(s)
GACT	Generally Available Control Technology
HAP	Hazardous Air Pollutant
HCFC	Hydrochlorofluorocarbon
HCl	Hydrochloric Acid
HFC	Hydrofluorocarbon
HSIA	Halogenated Solvents Industry Association
HPV	High Production Volume

Hr	Hour
IARC	International Agency for Research on Cancer
IDLH	Immediately Dangerous to Life and Health
i.p.	Intraperitoneal
IRIS	Integrated Risk Information System
ISHA	Industrial Safety and Health Act
kg	Kilogram(s)
L	Liter(s)
lb	Pound(s)
Log K_{oc}	Logarithmic Organic Carbon:Water Partition Coefficient
Log K_{ow}	Logarithmic Octanol:Water Partition Coefficient
m^3	Cubic Meter(s)
MACT	Maximum Achievable Control Technology
MCL	Maximum Contaminant Level
MCLG	Maximum Contaminant Level Goal
mg	Milligram(s)
µg	Microgram(s)
mmHg	Millimeter(s) of Mercury
MOA	Mode of Action
MSDS	Material Safety Data Sheet
n	Number
NAAQS	National Ambient Air Quality Standards
NAC	National Advisory Committee
NAICS	North American Industry Classification System
NCEA	National Center for Environmental Assessment
NEI	National Emissions Inventory
NESHAP	National Emission Standards for Hazardous Air Pollutants
NHANES	National Health and Nutrition Examination Survey
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NIH	National Institutes of Health
NIOSH	National Institute of Occupational Safety and Health
NITE	National Institute of Technology and Evaluation
NPL	National Priorities List
NTP	National Toxicology Program
OAQPS	Office of Air Quality Planning and Standards
OCSPP	Office of Chemical Safety and Pollution Prevention
ODS	Ozone Depleting Substance
OECD	Organisation for Economic Co-operation and Development
OEHHA	Office of Environmental Health Hazard Assessment
OEL	Occupational Exposure Limit
ONU	Occupational Non-User
OPPT	Office of Pollution Prevention and Toxics
OSHA	Occupational Safety and Health Administration
PBZ	Personal Breathing Zone
PCE	Perchloroethylene
PEL	Permissible Exposure Limit
PESS	Potentially Exposed Susceptible Subpopulation
POD	Point of Departure

POTW	Publicly Owned Treatment Works
ppb	Part(s) per Billion
PPE	Personal Protective Equipment
ppm	Part(s) per Million
PWS	Public Water System
RCRA	Resource Conservation and Recovery Act
SARA	Superfund Amendments and Reauthorization Act
SCHER	Scientific Committee on Health and Environmental Risks
SDS	Safety Data Sheet
SDWA	Safe Drinking Water Act
SIDS	Screening Information Data Set
SNAP	Significant New Alternatives Policy
STEL	Short-Term Exposure Limit
$t_{1/2}$	Half-life
TCCR	Transparent, Clear, Consistent, and Reasonable
TCE	Trichloroethylene
TLV	Threshold Limit Value
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TTO	Total Toxic Organics
TWA	Time-Weighted Average
U.S.	United States
VOC	Volatile Organic Compound
WHO	World Health Organization
Yr	Year(s)

EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the U.S. Environmental Protection Agency (EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). Perchloroethylene was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. In June 2017, EPA published the Scope of the Risk Evaluation for perchloroethylene. As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for perchloroethylene. Comments received on this problem formulation document will inform development of the draft risk evaluation.

This problem formulation document refines the conditions of use, exposures and hazards presented in the scope of the risk evaluation for perchloroethylene and presents refined conceptual models and analysis plans that describe how EPA expects to evaluate the risk for perchloroethylene.

Perchloroethylene, also known as ethene, 1,1,2,2-tetrachloro, tetrachloroethylene and PCE, is a high production volume (HPV) solvent. Perchloroethylene is subject to a number of federal and state regulations and reporting requirements. For example, perchloroethylene has been a Toxics Release Inventory (TRI) reportable chemical under Section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) since 1995. It is designated a Hazardous Air Pollutant (HAP) under the Clean Air Act (CAA), a hazardous waste under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) and a regulated drinking water contaminant under the Safe Drinking Water Act (SDWA).

Information on the domestic manufacture, processing and use of perchloroethylene is available to EPA through its Chemical Data Reporting (CDR) Rule, issued under TSCA. According to the 2016 CDR, more than 324 million pounds of perchloroethylene were manufactured (including imported) in the United States in 2015. According to the *Use and Market Profile for Tetrachloroethylene* (EPA-HQ-OPPT-2016-0732), perchloroethylene is primarily used to produce fluorinated compounds, such as hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs) (65%) followed by dry cleaning (15%) and vapor degreasing solvents (10%). Other uses can be quite varied, including:

- Adhesives
- Degreasing
- Brake cleaner
- Laboratories
- Lubricants
- Mold cleaners, releases and protectants
- Oil refining

- Sealants
- Stainless steel polish
- Tire buffers and cleaners and
- Vandal mark removers.

This document presents the potential exposures that may result from the conditions of use of perchloroethylene. Exposures may occur to workers and occupational non-users (workers who do not directly handle the chemical but perform work in an area where the chemical is used), consumers and bystanders (non-product users that are incidentally exposed to the product) and the general population through inhalation, dermal and oral pathways. Workers and occupational non-users (ONU), who do not directly handle the chemical but perform work in an area where the chemical is used, may be exposed to perchloroethylene during a variety of conditions of use, such as manufacturing, processing and industrial and commercial uses, including uses in degreasing and adhesives. EPA expects that the highest exposures to perchloroethylene generally involve workers in industrial and commercial settings. Perchloroethylene can be found in numerous products and can, therefore, result in exposures to commercial and consumer users in indoor or outdoor environments. For perchloroethylene, EPA considers workers, occupational non-users, consumers, bystanders, and certain other groups of individuals who may experience greater exposures than the general population due to proximity to conditions of use to be potentially exposed or susceptible subpopulations. Exposures to the general population may occur from industrial and/or commercial uses; industrial releases to air, water or land; and other conditions of use. EPA will evaluate whether groups of individuals within the general population may be exposed via pathways that are distinct from the general population due to unique characteristics (e.g., life stage, behaviors, activities, duration) that increase exposure and whether groups of individuals have heightened susceptibility, and should therefore be considered potentially exposed or susceptible subpopulations for purposes of the risk evaluation. EPA plans to further analyze inhalation exposures to vapors and mists for workers and occupational non-users and dermal exposures for skin contact with liquids in occluded situations for workers in the risk evaluation. For environmental release pathways, EPA plans to further analyze surface water exposure to aquatic vertebrates, invertebrates and aquatic plants and exposure to sediment-dwelling organisms.

Perchloroethylene has been the subject of several prior health hazard and risk assessments, including EPA's Integrated Risk Information System (IRIS) Toxicological Review and a draft Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile. A number of targets of toxicity from exposures to perchloroethylene have been identified in animal and human studies for both oral and inhalation exposures. EPA plans to evaluate all potential hazards for perchloroethylene, using the primary literature identified in human health reviews and including any found in recent literature. Hazard endpoints identified in previous assessments include: acute toxicity, neurotoxicity, kidney toxicity, liver toxicity, developmental and reproductive toxicity and cancer. Support for an association with immune and blood effects was less well characterized. Perchloroethylene is also considered to be irritating.

The revised conceptual models presented in this problem formulation identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); potentially exposed or susceptible subpopulations; and hazards EPA expects to consider in the risk evaluation. The initial conceptual models provided in the scope document were revised during problem formulation based on evaluation of reasonably available information for physical and chemical properties, fate, exposures, hazards and conditions of use, and based upon consideration of other statutory and regulatory authorities. In each problem formulation document for the first 10 chemical substances, EPA also

refined the activities, hazards and exposure pathways that will be included in and excluded from the risk evaluation.

EPA's overall objectives in the risk evaluation process are to conduct timely, relevant, high-quality, and scientifically credible risk evaluations within the statutory deadlines, and to evaluate the conditions of use that raise greatest potential for risk 82 FR 33726, 33728 (July 20, 2017).

1 INTRODUCTION

This document presents for comment the problem formulation of the risk evaluation to be conducted for perchloroethylene under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Frank R. Lautenberg Chemical Safety for the 21st Century Act amended the Toxic Substances Control Act (TSCA), the nation's primary chemicals management law, on June 22, 2016. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. The scope documents for all first 10 chemical substances were issued on June 22, 2017. The first 10 problem formulation documents are a refinement of what was presented in the first 10 scope documents. TSCA § 6(b)(4)(D) does not distinguish between scoping and problem formulation, and requires EPA to issue scope documents that include information about the chemical substance, including the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations that the Administrator expects to consider in the risk evaluation. In the future, EPA expects scoping and problem formulation to be completed prior to the issuance of scope documents and intends to issue scope documents that include problem formulation.

As explained in the scope document, because there was insufficient time for EPA to provide an opportunity for comment on a draft of the scope, as EPA intends to do for future scope documents, EPA is publishing and taking public comment on a problem formulation document to refine the current scope, as an additional interim step prior to publication of the draft risk evaluation for perchloroethylene. Comments received on this problem formulation document will inform development of the draft risk evaluation.

The Agency defines problem formulation as the analytical phase of the risk assessment in which "the purpose for the assessment is articulated, the problem is defined, and a plan for analyzing and characterizing risk is determined" (see Section 2.2 of the Framework for Human Health Risk Assessment to Inform Decision Making). The outcome of problem formulation is a conceptual model(s) and an analysis plan. The conceptual model describes the linkages between stressors and adverse human health effects, including the stressor(s), exposure pathway(s), exposed life stage(s) and population(s), and endpoint(s) that will be addressed in the risk evaluation (U.S. EPA, 2014e). The analysis plan follows the development of the conceptual model(s) and is intended to describe the approach for conducting the risk evaluation, including its design, methods and key inputs and intended outputs as described in the EPA Human Health Risk Assessment Framework (U.S. EPA, 2014e). The problem formulation documents refine the initial conceptual models and analysis plans that were provided in the scope documents.

First, EPA has removed from the risk evaluation any activities and exposure pathways that EPA has concluded do not warrant inclusion in the risk evaluation. For example, for some activities which were listed as "conditions of use" in the scope document, EPA has insufficient information following the further investigations during problem formulation to find they are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

Second, EPA also identified certain exposure pathways that are under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.

As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes.[1] EPA does not expect to include tany such excluded pathways as further explained below in the risk evaluation. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes.

Third, EPA identified any conditions of use, hazards, or exposure pathways which were included in the scope document and that EPA expects to include in the risk evaluation but which EPA does not expect to further analyze in the risk evaluation. EPA expects to be able to reach conclusions about particular conditions of use, hazards or exposure pathways without further analysis and therefore expects to conduct no further analysis on those conditions of use, hazards or exposure pathways in order to focus the Agency's resources on more extensive or quantitative analyses. Each risk evaluation will be "fit-for-purpose," meaning not all conditions of use will warrant the same level of evaluation and the Agency may be able to reach some conclusions without comprehensive or quantitative risk evaluations 82 FR 33726, 33734, 33739 (July 20, 2017).

EPA received comments on the published scope document for perchloroethylene and has considered the comments specific to perchloroethylene in this problem formulation document. EPA is soliciting public comment on this problem formulation document and when the draft risk evaluation is issued the Agency intends to respond to comments that are submitted. In its draft risk evaluation, EPA may revise the conclusions and approaches contained in this problem formulations, including the conditions of use and pathways covered and the conceptual models and analysis plans, based on comments received.

[1] As explained in the final rule for chemical risk evaluation procedures, "EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination." [82 FR 33726, 33734, 33729 (July 20, 2017)]

1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to perchloroethylene. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. EPA has evaluated and considered the impact of these existing laws and regulations (e.g., regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any, further analysis might be necessary as part of the risk evaluation. Consideration of the nexus between these existing regulations and TSCA conditions of use may additionally be made as detailed/specific conditions of use and exposure scenarios are developed in conducting the analysis phase of the risk evaluation.

Federal Laws and Regulations

Perchloroethylene is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

State Laws and Regulations

Perchloroethylene is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

Laws and Regulations in Other Countries and International Treaties or Agreements

Perchloroethylene is subject to statutes or regulations in countries other than the United States. A summary of these laws and regulations is provided in Appendix A.3.

1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations. Table 1-1 shows the assessments that have been conducted. This table includes one additional document identified since the publication of the Scope document from the Office of Health and Environmental Assessment.

In addition to using this information, EPA intends to conduct a full review of the relevant data/information collected in the initial comprehensive search [see *Perchloroethylene (CASRN 127-18-4) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0732)], using the literature search strategy [see *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document,* (EPA-HQ-OPPT-2016-0732)]. This will ensure that EPA considers data/information that has been made available since these assessments were conducted.

Table 1-1. Assessment History of Perchloroethylene

Authoring Organization	Assessment
EPA Assessments	
Integrated Risk Information System (IRIS)	Toxicological Review of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4) U.S. EPA (2012e)
Office of Air Quality Planning and Standards (OAQPS)	Perchloroethylene Dry Cleaners Refined Human Health Risk Characterization U.S. EPA (2005b)

Authoring Organization	Assessment
National Center for Environmental Assessment (NCEA)	Sources, Emission and Exposure for Trichloroethylene (TCE) and Related Chemicals U.S. EPA (2001c)
Office of Air Toxics	Tetrachloroethylene (Perchloroethylene); 127-18-4 U.S. EPA (2000b)
Office of Pesticides and Toxic Substances (now, Office of Chemical Safety and Pollution Prevention [OCSPP])	Occupational Exposure and Environmental Release Assessment of Tetrachloroethylene U.S. EPA (1985b)
Office of Health and Environmental Assessment	Final Health Effects Criteria Document for Tetrachloroethylene U.S. EPA (1985a)
Office of Water (OW)	Update of Human Health Ambient Water Quality Criteria: Tetrachloroethylene (Perchloroethylene) 127-18-4 U.S. EPA (2015b)
Office of Water (OW)	Ambient Water Quality Criteria for Tetrachloroethylene U.S. EPA (1980a)
Other U.S.-Based Organizations	
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment (OEHHA), Air Toxics Hot Spots Program	Perchloroethylene Inhalation Cancer Unit Risk Factor Cal/EPA (2016)
Agency for Toxic Substances and Disease Registry (ATSDR)	Toxicological Profile for Tetrachloroethylene (PERC) (Draft) ATSDR (2014)
National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee)	Tetrachloroethylene NAC/AEGL (2009)
California Environmental Protection Agency, OEHHA, Pesticide and Environmental Toxicology Section	Public Health Goal for Tetrachloroethylene in Drinking Water Cal/EPA (2001)
National Toxicology Program (NTP)	Toxicology and Carcinogenesis Studies of Tetrachloroethylene (Perchloroethylene); (CAS No. 127-18-4) in F344/N Rats and B6C3F1 Mice NTP (1986)
International	
International Agency for Research on Cancer (IARC)	IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Tetrachloroethylene IARC (2014b)
European Union (EU), Scientific Committee on Health and Environmental Risks (SCHER)	SCHER, Scientific Opinion on the Risk Assessment Report on Tetrachloroethylene, Human Health Part, CAS No.: 127-18-4, 12 SCHER (2008)

Authoring Organization	Assessment
World Health Organization (WHO)	Concise International Chemical Assessment Document 68: Tetrachloroethylene WHO (2006)
EU, European Chemicals Bureau (ECB)	EU Risk Assessment Report: Tetrachloroethylene, Part 1 - environment (2005a)
National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Australia	Tetrachloroethylene: Priority Existing Chemical Assessment Report No. 15 NICNAS (2001)

1.3 Data and Information Collection

EPA/OPPT generally applies a systematic review process and workflow that includes: (1) data collection (2) data evaluation and (3) data integration of the scientific data used in risk evaluations developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection may occur during the process of risk evaluation. Additional information that may be considered and was not part of the initial comprehensive bibliographies will be documented in the Draft Risk Evaluation for perchloroethylene.

Data Collection: Data Search

EPA/OPPT conducted chemical-specific searches for information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental and human exposures, including potentially exposed or susceptible subpopulations; ecological hazard, human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data and/or information potentially relevant to the risk evaluation. Generally, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). For human health hazard, EPA/OPPT relied on the search strategies from recent assessments, such as EPA Integrated Risk Information System (IRIS) assessments, to identify relevant information published after the end date of the previous search to capture more recent literature. The *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0732) provides details about the data and information sources and search terms that were used in the literature search.

Data Collection: Data Screening

Following the data search, references were screened and categorized using selection criteria outlined in the *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017d). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; human and environmental exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially

exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazard), but within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The supplemental document: *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document* discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic* (U.S. EPA, 2017d).

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information, for example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in supplemental document: *Strategy for Conducting Literature Searches for Perchloroethylene: Supplemental File for the TSCA Scope Document* and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review (U.S. EPA, 2017d).

Results of the initial search and categorization can be found in the supplemental document *Perchloroethylene (CASRN 127-18-4) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0732) (U.S. EPA, 2017b). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

1.4 Data Screening During Problem Formulation

EPA/OPPT is in the process of completing the full text screening of the on-topic references identified in the *Perchloroethylene (CASRN: 127-18-4) Bibliography: Supplemental File for the TSCA Scope Document* (U.S. EPA, 2017b). The screening process at the full-text level is described in the *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a). Appendix F provides the inclusion and exclusion criteria applied at the full text screening. The eligibility criteria are guided by the analytical considerations in the revised conceptual models and analysis plan, as discussed in the problem formulation document. Thus, it is expected that the number of data/information sources entering evaluation is reduced to those that are relevant to address the technical approach and issues described in the analysis plan of this document.

Following the screening process, the quality of the included data/information sources will be assessed using the evaluation strategies that are described in *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018b).

2 PROBLEM FORMULATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA included in the scope document a life cycle diagram and conceptual models that describe the actual or potential relationships between perchloroethylene and human and ecological receptors. During the problem formulation, EPA revised the conceptual models based on further data gathering and analysis as presented in this problem formulation document. An updated analysis plan is also included which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use of perchloroethylene.

2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1; EPA found no additional information during problem formulation that would change these values.

Table 2-1. Physical and Chemical Properties of Perchloroethylene

Property	Value[a]	References
Molecular formula	C_2Cl_4	
Molecular weight	165.833	
Physical form	Colorless liquid; ether-like, mildly sweet odor	Lewis (2007); NIOSH (2005); U.S. Coast Guard (1984)
Melting point	-22.3°C	Lide (2007)
Boiling point	121.3°C	Lide (2007)
Density	1.623 g/cm^3 at 20°C	Lide (2007)
Vapor pressure	18.5 mmHg at 25°C	Riddick et al. (1985)
Vapor density	5.7 (relative to air)	Browning (1965)
Water solubility	206 mg/L at 25°C	Horvath (1982)
Octanol:water partition coefficient (K_{ow})	3.40	Hansch et al. (1995)
Henry's Law constant	0.0177 atmm^3/mole	Gossett (1987)
Flash point	Not applicable	NFPA (2010)
Autoflammability	Not readily available	
Viscosity	0.839 cP @at 25°C	Hickman (2000)
Refractive index	1.4775	Lide (2007)
Dielectric constant	0 D	

[a] Measured unless otherwise noted.

2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as ''the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of.''

2.2.1 Data and Information Sources

In the scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. As further described in this document, EPA searched a number of available data sources (e.g., *Use and Market Profile for Tetrachloroethylene*, EPA-HQ-OPPT-2016-0732). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use [see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene) and Use*, EPA-HQ-OPPT-2016-0732] prior to a February 2017 public meeting on scoping efforts for risk evaluation convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public and stakeholder meetings has been incorporated into this problem formulation document to the extent appropriate. Thus, EPA believes the manufacture, processing, distribution, use and disposal activities identified in these documents constitute the intended, known, and reasonably foreseeable activities associated with the subject chemical, based on reasonably available information.

2.2.2 Identification of Conditions of Use

To determine the current conditions of use of perchloroethylene and inversely, activities that do not qualify as conditions of use, EPA conducted extensive research and outreach. This included EPA's review of published literature and online databases including the most recent data available from EPA's Chemical Data Reporting program (CDR) and Safety Data Sheets (SDSs). EPA also conducted online research by reviewing company websites of potential manufacturers, importers, distributors, retailers, or other users of perchloroethylene and queried government and commercial trade databases. EPA also received comments on the Scope of the Risk Evaluation for perchloroethylene (EPA-HQ-OPPT-2016-0732) that were used to determine the conditions of use. In addition, EPA convened meetings with companies, industry groups, chemical users, states, environmental groups, and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. Those meetings included a February 14, 2017 public meeting with such entities (EPA-HQ-OPPT-2016-0732).

EPA has removed from the risk evaluation any activities that EPA concluded do not constitute conditions of use – for example because EPA has insufficient information to find certain activities are circumstances under which the chemical is actually "intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of." EPA has also identified any conditions of use that EPA does not expect to include in the risk evaluation. As explained in the final rule for Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, TSCA Section 6(b)(4)(D) requires EPA to identify "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider" in a risk evaluation, suggesting that EPA is not required to consider all conditions of use, and EPA may exclude certain activities that EPA has determined to be conditions of use on a case-by-case basis 82 FR 33736, 33729 (July 20, 2017). For example, EPA may exclude conditions of use that the Agency has sufficient basis to conclude would present only de minimus exposures or otherwise insignificant risks (such as use in a closed system that effectively precludes exposure or as an intermediate).

The activities that EPA no longer believes are conditions of use or were otherwise excluded during problem formulation are described in Section 2.2.2.1. The conditions of use included in the scope of the risk evaluation are summarized in Section 2.2.2.2.

2.2.2.1 Categories and Subcategories Determined Not to be Conditions of Use During Problem Formulation

For perchloroethylene, EPA has conducted public outreach and literature searches to collect information about perchloroethylene's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with perchloroethylene. Based on the foregoing research and outreach, EPA does not have reason to believe that any categories or subcategories identified in the perchloroethylene scope should be excluded from the scope of the risk evaluation. Therefore, no categories or subcategories of use for perchloroethylene will be excluded from the scope of the risk evaluation.

Table 2-2. Categories and Subcategories Determined Not to be Conditions of Use During Problem Formulation

Life Cycle Stage	Category [a]	Subcategory [b]	References
No categories or subcategories have been excluded from the risk evaluation.			

2.2.2.2 Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

The uses of perchloroethylene include the production of fluorinated compounds, dry cleaning and vapor degreasing, as well as a number of smaller uses. Nearly 65% of the production volume of perchloroethylene is used as an intermediate in industrial gas manufacturing, more specifically to produce fluorinated compounds, such as hydrofluorocarbons (HFCs) and hydrochlorofluorocarbons (HCFCs) (NTP, 2014; ICIS, 2011). HFCs 134a and 125 are alternatives to chlorofluorocarbons (CFCs) and HCFCs, which are ozone depleting substances (ODSs), and the subject of a phase-out (https://www.epa.gov/ods-phaseout). HCFCs are transitional substances in the phase-out of ODSs (ICIS, 2011) (Public Comment, EPA-HQ-OPPT-2016-0732-0033). Previously, perchloroethylene was widely used to manufacture CFCs (esp. trichlorotrifluoroethane (CFC-113)) until production and importation of CFCs for most uses were phased out in the United States by regulations implementing the Montreal Protocol (40 CFR part 82). A relatively small amount of CFC-113 is still produced for exempted uses (teleconference with Honeywell, 2017; summary is available in the docket: EPA-HQ-OPPT-2016-0732).

The second largest use of perchloroethylene (~15%) is as a solvent in dry cleaning facilities (NTP, 2014). Perchloroethylene is non-flammable and effectively dissolves fats, greases, waxes and oils, without harming natural or human-made fibers. These properties enabled it to replace traditional petroleum solvents(ATSDR, 2014; Dow Chemical Co, 2008; Tirsell, 2000). The demand for perchloroethylene dry cleaning solvents has steadily declined as a result of the improved efficiency of dry cleaning equipment, increased chemical recycling and the popularity of wash-and-wear fabrics that eliminate the need for dry cleaning (ATSDR, 2014). Perchloroethylene is also used in dry cleaning detergent and dry cleaning sizing.

Approximately 60% of dry cleaning machines now use perchloroethylene as a solvent (DLI and NCA, 2017). In 1991, EPA estimated that 83% of all dry cleaning facilities used perchloroethylene as solvent (U.S. EPA, 1991). In 2008, the Halogenated Solvents Industry Association (HSIA) estimated that 70% of dry cleaners used perchloroethylene as dry cleaning solvent (EPA-HQ-OPPT-2016-0732-0027). Similarly, in 2011, King County, WA conducted a profile of the dry cleaning industry and found that 69% of respondents (105 of the 152 respondents) used perchloroethylene in their primary machine (Whittaker and Johanson, 2011). Hence, there appears to be a trend towards alternatives to perchloroethylene in dry cleaning. According to the dry cleaning industry, a majority of new perchloroethylene dry cleaning machines are sold in locations where local fire codes preclude the use of Class III combustible alternative solvents or where the nature of the dry cleaning operation requires the use of perchloroethylene (DLI and NCA, 2017).

The third most prevalent use of perchloroethylene (~10%) is as a vapor degreasing solvent (NTP, 2014). Perchloroethylene can be used to dissolve many organic compounds, select inorganic compounds and high-melting pitches and waxes making it ideal for cleaning contaminated metal parts and other fabricated materials (ATSDR, 2014). It is a very good solvent for greases, fats, waxes, oils, bitumen, tar and many natural and synthetic resins for use in chemical cleaning systems, degreasing light and heavy metals, degreasing pelts and leather (tanning), extraction of animal and vegetable fats and oils and textile dyeing (solvent for dye baths)(Stoye, 2000). Perchloroethylene is also used in cold cleaning, which is similar to vapor degreasing, except that cold cleaning does not require the solvent to be heated to its boiling point in order to clean a given component. Vapor degreasing and cold cleaning scenarios may include a range of open-top or closed systems, conveyorized/enclosed/inline systems, spray wands, dip containers and wipes.

Perchloroethylene has many other uses, which collectively constitute ~10% of the production volume. EPA's search of safety data sheets, government databases and other sources found over 375 products containing perchloroethylene. These uses include (but are not limited to):

- Adhesives
- Aerosol degreasing
- Brake cleaner
- Laboratories
- Lubricants
- Mold cleaners, releases and protectants
- Oil refining
- Sealants
- Stainless steel polish
- Tire buffers and cleaners
- Vandal mark removers

Many of these uses include consumer products, such as adhesives (arts and crafts, as well as light repairs), aerosol degreasing, brake cleaners, aerosol lubricants, sealants, sealants for gun ammunition, stone polish, stainless steel polish and wipe cleaners. The uses of perchloroethylene in consumer adhesives and brake cleaners are especially prevalent; EPA has found 16 consumer adhesive products and 14 consumer brake cleaners containing perchloroethylene [see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: Tetrachloroethylene (Perchloroethylene)* and *Use and Market Profile for Tetrachloroethylene*, EPA-HQ-OPPT-2016-0732-0003].

Table 2-3 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for perchloroethylene that EPA expects to consider in the risk evaluation. Using the 2016 CDR (U.S. EPA, 2016b), EPA identified industrial processing or use activities, industrial function categories and commercial and consumer use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For risk evaluations, EPA intends to consider each life cycle stage (and corresponding use categories and subcategories) and assess certain relevant potential sources of release and human exposure associated with that life cycle stage.

Beyond the uses identified in the *Scope of the Risk Evaluation for Perchloroethylene*, EPA has received no additional information identifying additional current conditions of use for perchloroethylene from public comment and stakeholder meetings.

Table 2-3. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage	Category [a]	Subcategory [b]	References
Manufacture	Domestic manufacture	Domestic manufacture	U.S. EPA (2016b)
	Import	Import	U.S. EPA (2016b)
Processing	Processing as a reactant or intermediate	Intermediate in industrial gas manufacturing	U.S. EPA (2016b); Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0013; Public Comment, Public Comment, EPA-HQ-OPPT-2016-0732-DRAFT-0018; Public Comment, Public Comment, EPA-HQ-OPPT-2016-0732-0033
		Intermediate in basic organic chemical manufacturing	U.S. EPA (2016b); Market Profile, EPA-HQ-OPPT-2016-0732;
		Intermediate in petroleum refineries	U.S. EPA (2016b); Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0018
		Residual or byproduct	Public Comment, EPA-HQ-OPPT-2016-0732-0013
	Incorporated into formulation, mixture or reaction product	Cleaning and degreasing products	U.S. EPA (2016b); Public Comment, EPA-HQ-OPPT-2016-0732-0017
		Adhesive and sealant products	U.S. EPA (2016b)
		Paint and coating products	U.S. EPA (2016b)
		Other chemical products and preparations	U.S. EPA (2016b)
	Incorporated into articles	Plastic and rubber products	Use Document, EPA-HQ-OPPT-2016-0732-0003
	Repackaging	Solvent for cleaning or degreasing	U.S. EPA (2016b)
		Intermediate	U.S. EPA (2016b)
	Recycling	Recycling	U.S. EPA (2016b)
Distribution in commerce	Distribution	Distribution	Use Document, EPA-HQ-OPPT-2016-0732-0003

Life Cycle Stage	Category [a]	Subcategory [b]	References
Industrial use	Solvents (for cleaning or degreasing)	Solvents and/or Degreasers (cold, aerosol spray or vapor degreaser; not specified in comment)	Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0022; Public Comment, EPA-HQ-OPPT-2016-0732-0029
		Batch vapor degreaser (e.g., open-top, closed-loop)	U.S. EPA (1985b); Public Comment, EPA-HQ-OPPT-2016-0732-0015; Public Comment, EPA-HQ-OPPT-2016-0732-0027
		In-line vapor degreaser (e.g., conveyorized, web cleaner)	U.S. EPA (1985b); Public Comment, EPA-HQ-OPPT-2016-0732-0014
	Solvents (for cleaning or degreasing)	Cold cleaner	Market Profile, EPA-HQ-OPPT-2016-0732; ; Public Comment, EPA-HQ-OPPT-2016-0732-0017
		Aerosol spray degreaser/cleaner	Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009; Public Comment, EPA-HQ-OPPT-2016-0732-0017
		Dry cleaning solvent	Market Profile, EPA-HQ-OPPT-2016-0732; U.S. EPA (2006a)
		Spot cleaner	Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009
	Lubricants and greases	Lubricants and greases (e.g., penetrating lubricants, cutting tool coolants, aerosol lubricants)	U.S. EPA (2016b); Market Profile, OBJ; Public Comment, EPA-HQ-OPPT-2016-0732-0027; Public Comment, EPA-HQ-OPPT-2016-0732-0029; Public Comment, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0027; Public

Life Cycle Stage	Category [a]	Subcategory [b]	References
			Comment, EPA-HQ-OPPT-2016-0732-0029
	Adhesive and sealant chemicals	Solvent-based adhesives and sealants	U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009; Public Comment, EPA-HQ-OPPT-2016-0732-0015; Public Comment, EPA-HQ-OPPT-2016-0732-0022; Public Comment, EPA-HQ-OPPT-2016-0732-0027
	Paints and coatings including paint and coating removers	Solvent-based paints and coatings, including for chemical milling	U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0006; Public Comment, EPA-HQ-OPPT-2016-0732-0009; Public Comment, EPA-HQ-OPPT-2016-0732-0015; Public Comment, EPA-HQ-OPPT-2016-0732-0020; Public Comment, EPA-HQ-OPPT-2016-0732-0027; Public Comment,EPA-HQ-OPPT-2016-0732-0062
	Processing aids, not otherwise listed	Pesticide, fertilizer and other agricultural chemical manufacturing	U.S. EPA (2016b)
	Processing aids, specific to petroleum production	Catalyst regeneration in petrochemical manufacturing	U.S. EPA (2016b); Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Dow Chemical Co (2008); Public Comment, EPA-HQ-OPPT-2016-0732-0018; Public Comment, EPA-HQ-OPPT-2016-0732-0027

Life Cycle Stage	Category [a]	Subcategory [b]	References
	Other uses	Textile processing	Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732
		Wood furniture manufacturing	Use Document, EPA-HQ-OPPT-2016-0732-0003
		Laboratory chemicals	Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0015
		Foundry applications	Use Document, EPA-HQ-OPPT-2016-0732-0003; Market Profile, EPA-HQ-OPPT-2016-0732
Commercial/consumer use	Cleaning and furniture care products	Cleaners and degreasers (other)	Market Profile, EPA-HQ-OPPT-2016-0732; Public Comment, EPA-HQ-OPPT-2016-0732-0009; Public Comment, EPA-HQ-OPPT-2016-0732-0017; Public Comment, EPA-HQ-OPPT-2016-0732-0022; EPA-HQ-OPPT-2016-0732-0023; Public Comment, EPA-HQ-OPPT-2016-0732-0027; Public Comment, EPA-HQ-OPPT-2016-0732-0029
		Dry cleaning solvent	Market Profile, EPA-HQ-OPPT-2016-0732; U.S. EPA (2006a); Public Comment, EPA-HQ-OPPT-2016-0732-0007; Public Comment, EPA-HQ-OPPT-2016-0732-0009
		Spot cleaner	Market Profile, EPA-HQ-OPPT-2016-0732; U.S. EPA (2006a); Public Comment, EPA-HQ-OPPT-2016-0732-0009
		Automotive care products (e.g., engine degreaser and brake cleaner)	U.S. EPA (2016b), Use Document, EPA-HQ-OPPT-2016-0732-0003; Market